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Tesis doctoral

Social and behavioural determinants of health: studies on HIV, sexually transmitted infections, and mental health

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I hope this thesis can contribute to improving the lives of people living with HIV, men who have sex with men and people with mental health disorders. Focusing on the social determinants of health, I hope this thesis can contribute towards health equity and social justice.

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1. Introduction

2. Studies

Abstract

The health and well-being of individuals and communities are profoundly determined by a complex interplay of the contexts and conditions in which they live. These factors, known as social and structural determinants of health, encompass non-medical aspects that impact health outcomes. They include the conditions in which people are born, grow, work, live, and age, as well as the broader forces and systems shaping their daily lives. Additionally, individual lifestyle choices and behaviours can either promote or put health at risk, referred to as behavioural determinants, which are influenced by both individual factors, such as genetics and personality, and social and structural determinants. Variations in social and structural conditions among individuals and communities can result in significant disparities in health outcomes. By addressing these determinants, we can foster health equity and create conditions that enable all individuals to lead healthy and fulfilling lives.

This dissertation investigates social, structural, and behavioural determinants of health through five studies focused on HIV, sexually transmitted infections (STIs), and mental health during the COVID-19 pandemic. These five studies provide quantitative evidence for the role of different social and behavioural aspects in determining public health and epidemiological outcomes in these disease areas. The studies report factors at the micro- and macro-levels that contribute to health inequalities, identifying potential intervention areas to improve health outcomes and promote health equity.

The first study examines social and behavioural determinants of syphilis among men who have sex with men (MSM) across 31 countries in Europe. This study highlights the contribution of social and behavioural factors to rising syphilis diagnoses in Europe, such as STI screening practices the number of non-steady male condomless anal intercourse partners, engagement in sex work, and the use of pre-exposure prophylaxis. The study identifies strengthened regular screening as a potential key interventional area for syphilis control and its implementation feasibility in HV pre-exposure prophylaxis (PrEP) clinical guidelines.

The second study offers methodological insights into a crucial behavioural determinant of STIs and HIV transmission rates: the number of sexual partners. The study offers insights into designing sexual behaviour surveys that accurately measure the number of sexual partners among MSM and understand biases associated with alternative approaches. The

results provide, first, an empirical basis for converting banded ordinal data on numbers of sex partners into a continuous scale-level variable. Second, it provides evidence on the distribution and clustering of responses about the number of sexual partners, showing that some individuals report a high number of partners above common cut-off values used in surveys.

The third study investigates HIV-related stigma and discrimination, its sociodemographic determinants and its impact on HIV testing uptake in 64 low- and middle-income countries. The results reveal the wide prevalence of stigma, albeit with varying degrees across countries. Results show a social gradient in holding stigmatizing attitudes, as well as an association between stigma and lower HIV testing uptake, highlighting the need for targeted interventions to eliminate stigma for improving the quality of life of people with HIV and as a means of HIV elimination.

The fourth study assesses the impact of national HIV treatment guidelines as a structural determinant of HIV outcomes in 37 countries in Europe and Central Asia. The study demonstrates the population-level benefits of implementing ‘test-and-treat’ antiretroviral therapy (ART) guidelines, which recommend initiation of ART upon diagnosis regardless of CD4 cell count, which improve ART access and viral suppression and reduce HIV transmission, further strengthening evidence that rapid initiation of treatment helps curb the spread of HIV.

Finally, the fifth study investigates the role of national social protection systems and pandemic-specific measures on mental health well-being during the COVID-19 pandemic in 26 European countries. The study reveals that the COVID-19 pandemic has led to substantial mental health deterioration in older adults, particularly among socioeconomically disadvantaged individuals. Physical distancing measures exacerbated this decline, while stronger social protection decreased the risk of mental health worsening, emphasizing the importance of robust social support systems for mental health, particularly during crises.

Overall, the findings from these studies underscore the importance of addressing the social, structural, and behavioural determinants of health and implementing evidence-based comprehensive disease prevention and health promotion interventions to improve health and well-being.

Resumen

La salud y el bienestar de las personas y las comunidades están profundamente determinados por una compleja interacción de los contextos y las condiciones en que viven. Estos contextos y condiciones que influyen en nuestra salud son los determinantes sociales y estructurales de la salud, factores no médicos que influyen en los resultados sanitarios. Estos determinantes incluyen las condiciones en que las personas nacen, crecen, trabajan, viven y envejecen, y el conjunto más amplio de fuerzas y sistemas que configuran las condiciones de la vida cotidiana. Nuestros estilos de vida y nuestros comportamientos también pueden favorecer o poner en riesgo la salud: estos son los determinantes conductuales de la salud, los cuales están influenciados por factores individuales, como la genética y la personalidad, así como también por las condiciones sociales y estructurales en las que una persona vive. Las condiciones sociales y estructurales pueden variar substancialmente entre individuos y comunidades. La exposición a diferentes condiciones y contextos puede dar lugar a profundas disparidades en la salud. Al abordar estos determinantes, podemos promover la equidad en salud y crear condiciones que permitan a todas las personas llevar una vida sana y plena.

Esta tesis investiga determinantes sociales, estructurales y conductuales de la salud en cinco estudios que abarcan el VIH, las infecciones de transmisión sexual (ITS) y la salud mental durante la pandemia COVID-19. Estos estudios aportan evidencia cuantitativa del papel de distintos aspectos sociales y conductuales en la determinación de los resultados epidemiológicos y de salud pública. Se examinan factores, a nivel micro y macro, que contribuyen a la generación desigualdades en salud, identificando posibles ámbitos de intervención para promover la salud y la equidad sanitaria.

El primer estudio examina los determinantes sociales y conductuales de la sífilis en la población de hombres que tienen sexo con hombres (HSH) en 31 países europeos. El estudio evidencia la contribución de los factores sociales y conductuales en el aumento de los diagnósticos de sífilis en Europa, como las prácticas de cribado de ITS, el número de parejas sexuales (particularmente relaciones sexuales anales sin preservativo con parejas no estables), la participación en el trabajo sexual y el uso de profilaxis preexposición (PrEP). El estudio identifica el refuerzo del cribado periódico como un potencial área clave de intervención para el control de la sífilis y su viabilidad de implementación en las directrices clínicas de la PrEP.

El segundo estudio ofrece información metodológica sobre un determinante conductual clave de las tasas de transmisión del VIH e ITS: el número de parejas sexuales. El estudio ofrece ideas para diseñar encuestas de comportamiento sexual que midan con precisión el número de parejas sexuales entre los HSH y comprendan los sesgos asociados a enfoques alternativos. Los resultados proporcionan, en primer lugar, una base empírica para convertir los datos sobre el número de parejas sexuales medidos con una variable ordinal con rangos en una variable continua de escala. En segundo lugar, aporta pruebas sobre la distribución y agrupación de las respuestas sobre el número de parejas sexuales, mostrando que algunos individuos declaran un número elevado de parejas por encima de los valores de corte habituales utilizados en las encuestas.

El tercer estudio investiga el estigma y la discriminación asociados al VIH, sus determinantes sociodemográficos y su impacto en la realización de pruebas del VIH en 64 países de ingresos bajos y medios. Los resultados revelan la amplia prevalencia de la estigmatización asociada al VIH, aunque con distintos grados según el país. Los resultados muestran un gradiente social en el mantenimiento de actitudes estigmatizantes, así como una asociación entre el estigma y una menor realización de las pruebas del VIH, lo que pone de relieve la necesidad de intervenciones específicas para eliminar el estigma con el fin de mejorar la calidad de vida de las personas con VIH y como medio para la eliminación del VIH.

El cuarto estudio evalúa el impacto de las guías nacionales de práctica clínica de tratamiento del VIH como determinante estructural de los resultados del VIH en 37 países de Europa y Asia Central. El estudio demuestra los beneficios a nivel poblacional de la aplicación de las directrices de terapia antirretroviral (TAR) de "prueba y tratamiento" (‘test-and-treat’), que recomiendan el inicio de la TAR tras el diagnóstico independientemente del recuento de células CD4, mejorando el acceso a la TAR y la supresión vírica y reduciendo la transmisión del VIH, reforzando la evidencia de que el inicio rápido del tratamiento ayuda a frenar la propagación del VIH.

Por último, el quinto estudio investiga el papel de los sistemas nacionales de protección social y las medidas tomadas en respuesta a la pandemia en el estado de la salud mental durante la pandemia COVID-19 en 26 países europeos. El estudio revela que la pandemia de COVID-19 ha provocado un deterioro sustancial de la salud mental de los adultos mayores, sobre todo entre las personas socioeconómicamente desfavorecidas. Las medidas de distanciamiento físico agravaron este deterioro, mientras que una mayor protección social disminuyó el riesgo de empeoramiento de la salud mental, lo que pone de relieve la importancia de contar con sólidos sistemas de apoyo social para la salud mental, especialmente durante las crisis.

Los resultados de estos estudios subrayan la importancia de abordar los determinantes sociales, estructurales y conductuales de la salud y de aplicar intervenciones integrales de prevención de enfermedades y promoción de la salud basadas en evidencia para mejorar la salud y el bienestar.

1. Introduction

1.1 Background

Social, structural, and behavioural determinants of health

The health of individuals and communities is influenced by a multitude of factors that intersect and intertwine. The context and conditions in which we live as well as our genetic makeup, behaviours, and the physical and biomedical environment are factors that have a significant role in determining whether we are healthy or not.[1] The non-biomedical contexts and conditions that influence our health are the social determinants of health. These determinants encompass a wide range of interrelated aspects, such as social and economic factors, living conditions, individual behaviours, social policies, political systems, and access to healthcare services, among others.

Social conditions often vary greatly between individuals and communities. These differences provide strong indications to explain profound disparities in health outcomes. Differential health outcomes result in a social gradient of health, whereby individuals' social and economic positions significantly influence their health.[2-4] The social gradient of health manifests as a consistent pattern where individuals in advantaged socioeconomic positions tend to enjoy better health, while those in lower socioeconomic positions face higher risks of poor health.[2-4] This pattern holds across various measures of health, including mortality rates, disease incidence and prevalence, and overall well-being.

This gradient is also evident in the varying health outcomes across different nations.[2-4] Countries with greater income equality, social cohesion, stronger social welfare systems, and greater investments in education and healthcare tend to exhibit better population health outcomes and a flatter social gradient of health, indicating a more equitable distribution of health outcomes across their populations, compared to countries with higher levels of inequality.[2-4] The social gradient of health highlights the profound role of social determinants of health in influencing the stark disparities in health between individuals, communities, and countries.

The social determinants of health, according to the World Health Organization (WHO), are the complex and overlapping "*conditions in which people are born, grow, work, live, and age*".[5] Social determinants of health refer to the social, economic, and political factors that shape an individual's living conditions and access to resources. These determinants include, for example, income and wealth, education, employment opportunities, social support networks, and community cohesion, among others. Social determinants have a profound impact on health outcomes and well-being as they can create conditions that either support or hinder individuals' ability to lead healthy lives. For example, individuals with low socioeconomic status often face greater challenges in accessing nutritious food, safe housing, and quality healthcare.[2,3] They may also be more likely to experience chronic stress, limited social support, and discrimination, which can contribute to poor health outcomes such as higher rates of chronic diseases, mental health disorders, and reduced life expectancy.[2,3]

The structural determinants of health refer to a particular type of social determinants: they are the broader social, economic, and political systems that shape the distribution of resources and power within a society. The WHO definition of social determinants alludes to the structural determinants of health when referring to the "*wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies and political systems.*"[5] These determinants include policies, laws, and institutional practices that can either promote or impede health and well-being. For instance, policies related to housing, transportation, and urban planning can influence the availability of safe and affordable housing, access to healthy food options, and opportunities for physical activity.[2,3] Structural determinants also encompass broader societal factors such as racism, sexism, and other forms of discrimination, which can create systemic barriers to health equity. Marginalized populations, such as racial and ethnic minorities, lesbian, gay, bisexual, transgender, queer (LGBTQ+) individuals, and people with disabilities, often face disproportionate health disparities due to structural inequalities.

Behavioural determinants of health refer to the acts and conducts that constitute the lifestyle and choices that either promote or put health at risk.[6] Given the interlinked nature of the determinants of health, these choices and behaviours are shaped by social and structural determinants, as well as individual factors, such as genetics and personality. Examples of behavioural determinants include diet and nutrition choices, physical activity, substance use, sexual behaviour, and adherence to preventive measures such as vaccinations and regular health screenings. Individual behaviours are influenced by a multitude of factors, including social norms, cultural practices, and personal beliefs. While individual behaviour plays a crucial role in health outcomes, it is important to recognize that behaviour is shaped and influenced by social and structural factors. For example, individuals living in neighbourhoods with limited access to healthy food options may have difficulty adopting a nutritious diet.[6] Similarly, individuals facing economic insecurity may engage in unhealthy coping behaviours such as smoking or excessive alcohol consumption.[6]

The negative consequences and inequities arising from some of these determinants can sometimes be avoided. Some social, structural, and behavioural determinants can be actively influenced and modified to improve health and prevent disease. Addressing the social and structural determinants of health requires, nonetheless, comprehensive policy changes and systemic reforms with collaborations across various sectors. Yet, the benefit can be immense, as it is possible to reduce health disparities, improve overall population health, and prevent many diseases and health conditions. Possible initiatives include, for instance, promoting equitable distribution of resources, reducing income inequality, providing quality education and employment opportunities, and promoting cohesion and inclusion. Changes can focus on eliminating discriminatory practices and advocating for policies that support health equity. Addressing behavioural determinants of health requires a comprehensive approach that combines individual-level interventions with broader social and structural modifications. Effective strategies include health education and promotion campaigns, policies to regulate unhealthy behaviours, and creating supportive environments that enable individuals to make healthier choices. Investigating and understanding the social, structural, and behavioural determinants of health is a crucial first step for effectively promoting better and more equitable population health and well-being.

This dissertation investigates social, structural, and behavioural determinants of health through five studies focused on HIV, sexually transmitted infections (STIs), and mental health during the COVID-19 pandemic. These five studies provide quantitative evidence for the role of different social and behavioural aspects in determining public health and epidemiological outcomes in these disease areas. The studies report factors at the micro- and macro-levels that contribute to health inequalities, identifying potential intervention areas to improve health outcomes and promote health equity. The first study examines social and behavioural determinants of syphilis among men who have sex with men (MSM) across 31 countries in Europe. The second study offers methodological insights into a crucial behavioural determinant of STIs and HIV transmission rates: the number of sexual partners. The third study assesses the impact of national HIV treatment guidelines as a structural determinant of HIV outcomes in 37 countries in Europe and Central Asia. The fourth study investigates HIV-related stigma and discrimination, its sociodemographic determinants and its impact on HIV testing uptake in 64 low- and middle-income countries. Finally, the fifth study investigates the role of national social protection systems and pandemic-specific measures on mental health well-being during the COVID-19 pandemic in 26 European countries.

The following introduction provides succinct background information on HIV and STIs, including basic information on the epidemiology of the diseases, with a focus on Europe, (given the same focus in some of the included studies). Then, another section covers background information on COVID-19 and mental health. This introduction serves as a general background to the more focused introductions of each study.

HIV and sexually transmitted infections

General facts and epidemiology

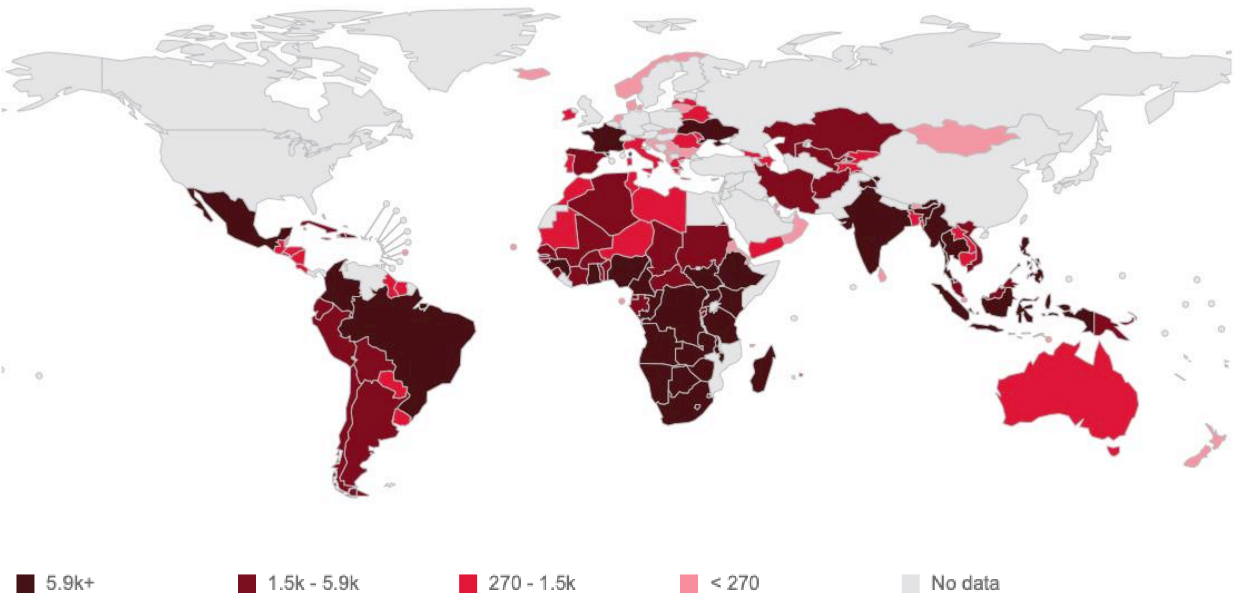
Human immunodeficiency virus (HIV) and sexually transmitted infections (STIs) are significant public health issues globally. The World Health Organization (WHO) estimated in 2020 that globally, there are each year over 374 million new cases of the four most common curable STIs: gonorrhoea (82 million), chlamydia (129 million), syphilis (7.1 million), and trichomoniasis (156 million), with 1 million new infections occurring every day.[7] HIV, on the other hand, affected in 2022 39.0 million [33.1–45.7 million]people worldwide, with approximately 1.3 million [1.0–1.7 million] new infections each year.[8] These infections can affect the quality of life and life expectancy of infected individuals. Yet, these infections not only affect the physical health of individuals but also have significant social and economic consequences.

STIs have a substantial burden of disease, impacting reproductive and sexual health as well as causing other major adverse health outcomes.[7,9] STIs also increase infectiousness and susceptibility to HIV.[7,9] There are more than 30 known pathogens, including bacteria, viruses, and parasites, to be transmitted from an infected person to a non-infected person through the exchange of body fluids such as semen and vaginal secretions through sexual contact, namely vaginal, anal, and oral sex.[7,9] STIs, such as chlamydia, gonorrhoea, syphilis, and HIV are among the most common infections transmitted through sexual contact.[7,9] Additionally, many STIs can also be transmitted vertically from mother to child during pregnancy and delivery, and some STIs can also be spread through the exchange of blood and blood products. Early diagnosis, treatment, and care can prevent the development of reproductive and sexual health complications, curing the disease among curable diseases (for instance, with a regimen of antibiotics) or modulating the disease course of incurable infections.[7,9] Early diagnosis and treatment can also prevent onward transmission of STIs.[7,9]

Syphilis is among the most common curable STIs.[10,11] Syphilis is a bacterial STI caused by Treponema pallidum, a motile Gram-negative spirochaete. Syphilis can also be transmitted via blood transfusions and from mother-to-child during pregnancy.[10,11] The disease develops in stages with different symptoms.[10,11] Early treatment can cure the disease yet it cannot undo any damages that may have already occurred.[10,11] If untreated, syphilis can result in a substantial burden of disease, causing serious health problems affecting different organ systems and leading to different adverse health outcomes, such as vision and hearing loss, cardiovascular and neurological diseases, congenital abnormalities, adverse pregnancy outcomes, and death.[10,11] Syphilis infection also increases the risk of HIV acquisition.[10,11]

HIV is an infection that attacks the immune system.[8,12,13] Acquired immunodeficiency syndrome (AIDS) is the most advanced stage of the disease, where the immune system is severely damaged by the virus and can cause death.[8,12,13] HIV makes a person more susceptible to other diseases, including non-communicable diseases, such as cancers, and infectious diseases, such as tuberculosis and other infections, as well as causing these other diseases to get worse.[8,12,13] In addition to sexual transmission, HIV can be transmitted through the exchange of body fluids such as blood and breastmilk through, respectively, sharing needles, syringes, and other drug injection equipment, as well as during the perinatal period via maternal-to-child transmission during pregnancy, childbirth, and breastfeeding.[8,12,13] While incurable, early diagnosis and treatment of HIV with antiretroviral therapy (ART) can modulate the course of HIV making it a manageable condition with which people living with HIV (PLHIV) can live long and healthy lives. Further, ART can suppress the virus making HIV undetectable, which makes it untransmittable, thus preventing onward transmission.[8,12,13]

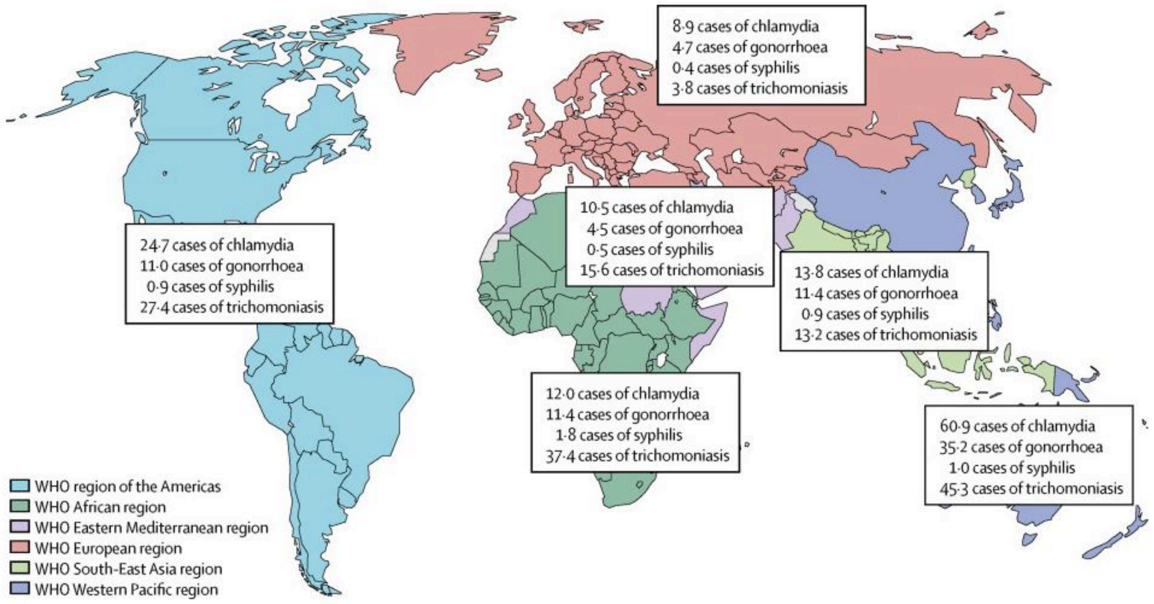
Figure 1. National trend of new HIV infections for the period 2010-2021.



Reprinted from UNAIDS, AidsInfo[14]

The HIV epidemic and multiple STI epidemics disproportionally affect low-income and middle-income countries.[9,12,13] The majority of new HIV infections occur in sub-Saharan Africa, where two-thirds of all new HIV infections occur, and where the prevalence of HIV is the highest.[8,14] However, other regions, including Europe, are also affected by new HIV infections (Figure 1). In Europe, the incidence of HIV is relatively low compared to other world regions. New HIV cases occur particularly in the Eastern part of the region.[15] The incidence of STIs also varies substantially across world regions (Figure 2). In contrast to HIV incident cases, which have declined from 2.2 million in 2010 to 1.3 million in 2022,[8] the overall total number of incident cases of the four most common STIs have increased over the past three decades and there are alarming increases in antimicrobial resistance in gonorrhoea and mycoplasma.[16,17] No major changes in STIs incidence rates have occurred in the past three decades, with nearly stable levels of changes in incidence rates.[18,19]

Figure 2. Regional incidence of the four most common sexually transmitted infections, 2012.



Reprinted from Unemo et al. *Sexually transmitted infections: challenges ahead*, Lancet Infectious Diseases (2017).

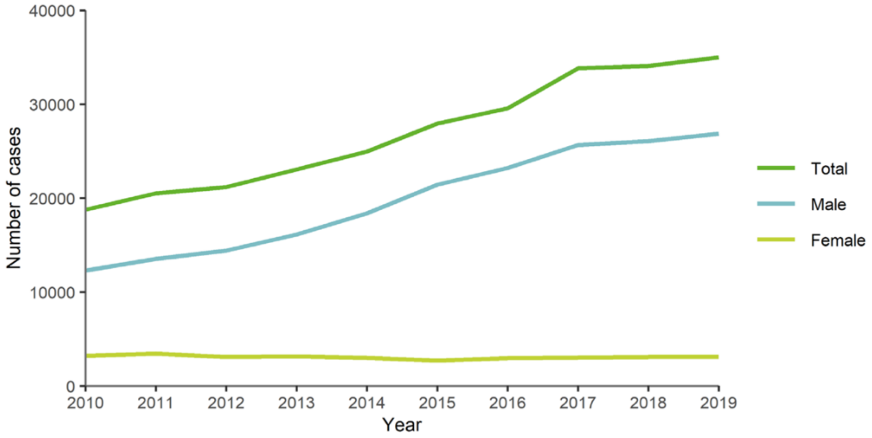
Social, behavioural, and structural dimensions of HIV and STIs

The burden of STIs and HIV is not evenly distributed across populations, with certain groups being at higher risk of infection than others. In general, STIs and HIV disproportionately affect marginalized and vulnerable populations, such as sex workers, men who have sex with men (MSM), transgender individuals, people who inject drugs, people in prisons, migrants, and young people.[20] For instance, in Western Europe, HIV and syphilis are a syndemic highly concentrated in the population of MSM.[9,15] While syphilis incident cases remained at a low level among women and heterosexual individuals, the number of syphilis cases among MSM has increased steeply in the last decade (Figure 3).[15] Similarly, new HIV diagnoses in Western Europe with known mode of transmission are disproportionally concentrated in the population of MSM (Figure 4).[15]

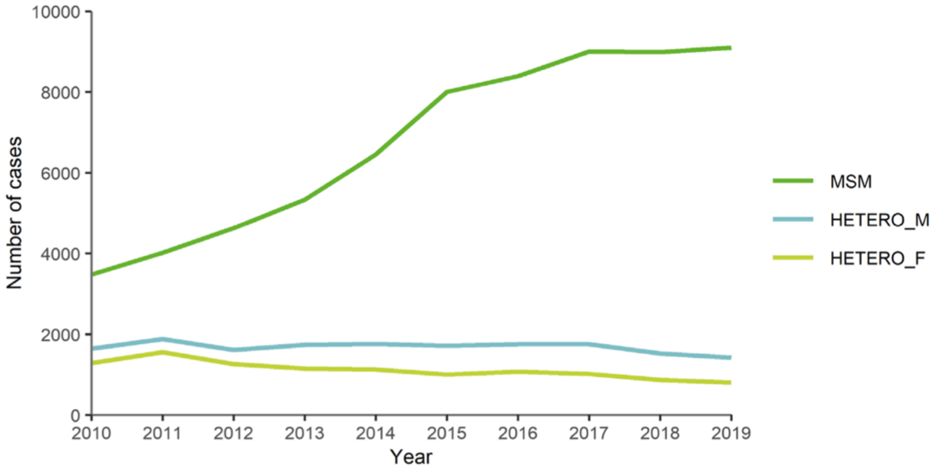
These key population groups face a range of social, economic, and legal barriers that limit their access to information, prevention, and treatment services for HIV and STIs.[20,21] Additionally, the stigma and discrimination associated with these infections often prevent individuals from seeking care and support, further exacerbating the spread of these infections.[22]

Figure 3. New syphilis cases in the European Union (EU) and European Economic Area (EEA) countries.

a. Number of confirmed syphilis cases by gender and year in EU/EEA countries reporting consistently, 2010−2019

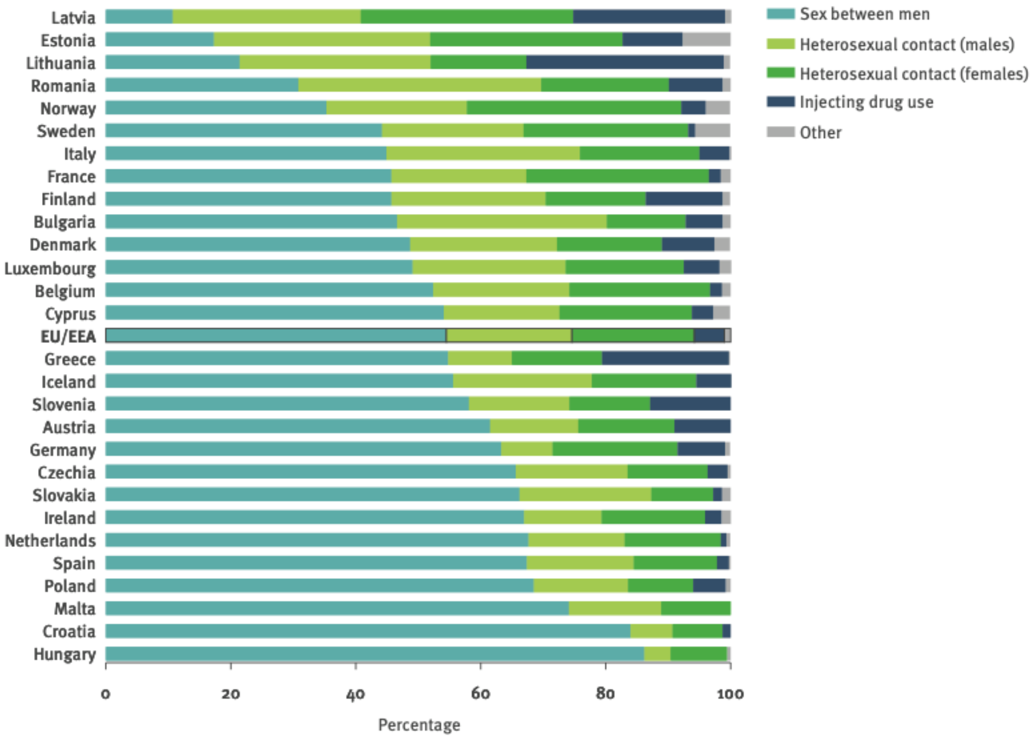


b. Number of confirmed syphilis cases by gender, transmission category and year in EU/EEA countries reporting consistently, 2010−2019



Reprinted from European Centre for Disease Prevention and Control (ECDC), *Syphilis - Annual Epidemiological Report for 2019*. Solna: ECDC (2022).[15]

Figure 4. Percentage of new HIV diagnoses with known mode of transmission, by transmission route and country, EU/EEA, 2021 (n = 12,205)



Reprinted from WHO Regional Office for Europe, European Centre for Disease Prevention and Control. *HIV/AIDS surveillance in Europe 2022 – 2021 data*. Copenhagen: WHO Regional Office for Europe (2022).[15]

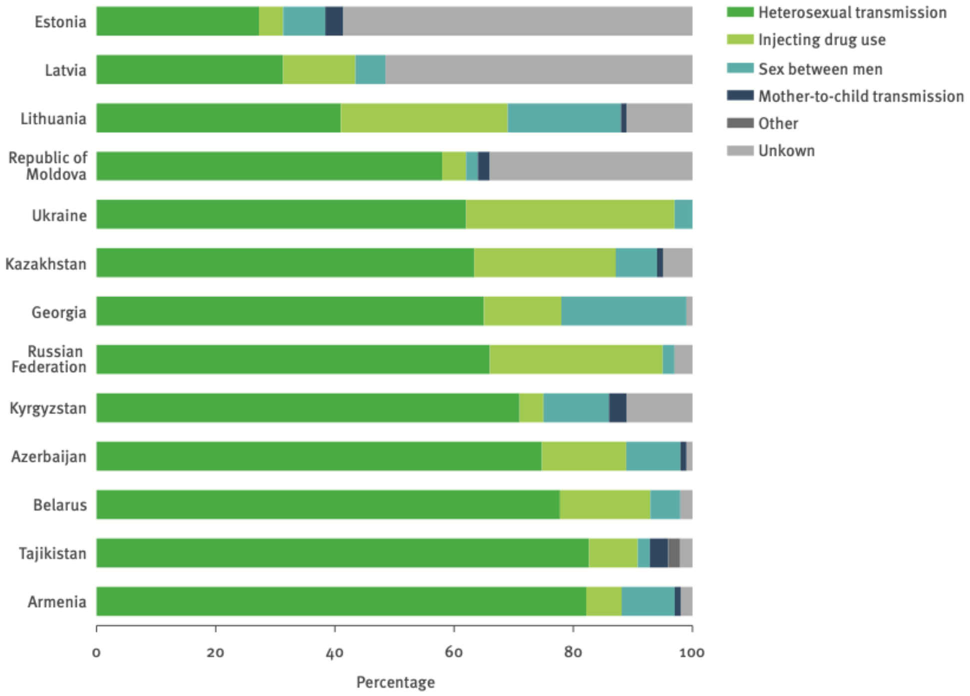
The transmission of STIs and HIV is influenced by a range of biological, behavioural, and social factors. Social and behavioural determinants of HIV and STIs include factors such as risky sexual behaviour, drug use, and poor sexual health literacy.[7,8] In addition, structural factors such as poverty, lack of access to healthcare services, gender inequality, and stigma, among others, also contribute to the transmission and spread of these infections.[7,8]

Sexual behaviour is one of the primary determinants of HIV and other STIs transmission.[7,8] The number of sexual partners, frequency of sexual activity, use of condoms, and engagement in high-risk sexual activities such as unprotected (i.e. condomless) sex, especially anal sex, all influence the risk of infection.[7,8] For example, having multiple sexual partners increases the likelihood of being exposed to HIV and other STIs. Thus, condom use is a vital preventative measure, reducing the risk of transmission by creating a physical barrier. In contrast, condomless anal sex is considered a high-risk activity as it increases the likelihood of exposure to HIV and other STIs. Increased risk with anal condomless sex responds to the difference in the anal and vaginal anatomy, being the rectal mucosa a vulnerable tissue more receptive to HIV and STIs.[23]

Additionally, substance use is another significant determinant of HIV and other STIs transmission.[7,8] Substance use can impair judgement and lead to risky sexual behaviour, which can increase the risk of acquiring HIV and other STIs. Substance use also leads to lower rates of presentation and retention in care and treatment discontinuation.[7,8,24] The use of drugs during sexual activities, chemsex, has been associated with an increased risk of STI and HIV transmission due to factors such as multiple sexual partners and reduced condom use.[25,26] If drugs are injected, this can expose individuals to HIV and other STIs through the sharing of needles or other injection equipment. Injecting drug use (IDU) is a major transmission mode of HIV in some countries.[15] For instance, in some countries in Eastern Europe it represents up to 1 of every 3 or 4 cases, such as in the Russian Federation and Ukraine.[15] IDU is also a significant mode of HIV transmission in the EU/EEA area in countries like Greece, Lithuania, and Latvia (Figure 4 and Figure 5).[15] Substitution maintenance therapy in the management of opioid dependence and needle and syringe exchange programmes are effective treatments for addiction to opioid drugs and for the prevention of the spread of HIV.[27,28] Many countries have developed policies and made investments for the implementation of these types of harm reduction programmes. Yet, in certain countries, such as the Russian Federation, these policies have not been implemented despite the scientific evidence and human rights implications, fostering the HIV epidemic.[29-31] Policy decisions like these represent structural determinants of the HIV and STIs epidemics.

Access to healthcare services can influence the spread of HIV and other STIs, particularly services such as HIV and STIs testing, treatment, and prevention services, which can help prevent disease and onward transmission rates.[7,8] Lack of access to healthcare can lead to untreated infections and increased risk of transmission.[7,8] Preventive interventions are also an essential tool in reducing the spread of HIV and other STIs. Interventions such as condom distribution programs, needle exchange programs, access to contraception, and pre-exposure prophylaxis (PrEP) can help reduce the risk of HIV and other STIs transmission.[8,12,13] Condom distribution programs can make them readily available to those who may not have access otherwise. PrEP is a medication that can be taken to reduce the risk of HIV infection for individuals who are at high risk of exposure by preventing the virus from taking hold. Given the increased burden of other diseases among people living with HIV and STIs, access to healthcare services non-specific to HIV and STIs can help improve the quality of life.[32,33]

Figure 5. New HIV diagnoses, by country and transmission mode, East, 2021 (n = 83,438)



Reprinted from WHO Regional Office for Europe, European Centre for Disease Prevention and Control. *HIV/AIDS surveillance in Europe 2022 – 2021 data*. Copenhagen: WHO Regional Office for Europe (2022).[15]

Societal norms and cultural beliefs regarding sexual behaviour and drug use can influence the risk of HIV and STIs transmission.[7,8,22] For example, in some cultures, condom use may be stigmatized or discouraged, which can increase the risk of transmission.[34,35] Stigma and discrimination against individuals living with HIV and other STIs can discourage individuals from seeking testing and treatment, which can lead to increased transmission rates.[22] HIV-related stigma and discrimination, coupled with stigma and criminalization of lesbian, gay, bisexual, transexual, queer, intersexual, and other (LGBTQI+) individuals and sex workers, deepens further these epidemics.[21] These societal attitudes and legal frameworks create barriers to accessing vital healthcare services and contribute to the vulnerability of these marginalized communities.[22] Stigma leads to social exclusion, hindering individuals from seeking prevention methods and testing.[22] Criminalization forces these activities underground, promoting individuals to have and be exposed to riskier behaviours.[22,36] Discrimination by healthcare providers further discourages seeking timely treatment and counselling.[22]

Education and awareness interventions can help individuals understand the risks of HIV and other STIs, and promote behaviours that can reduce the risk of transmission.[7] They can also help reduce stigma and discrimination against individuals living with HIV and other STIs as well as towards key populations.[37,38] These interventions can target specific populations, such as adolescents, who may be at increased risk of HIV and other STIs transmission due to inexperience or lack of knowledge. They can also be tailored to specific cultural or religious beliefs that may influence sexual behaviour and risk-taking. By eliminating laws that discriminate, societies can address the structural barriers that hinder effective HIV and STIs prevention and control efforts.[21,22] This approach promotes human rights, social justice, and equality, and contributes to ending the epidemics by ensuring that all individuals have equal access to the necessary healthcare services and support.

Multiple other factors from the above constitute social, structural, and behavioural determinants of the HIV and STIs epidemics. For instance, other key factors shaping the HIV and STIs epidemics include, among others, race and ethnic inequalities, gender inequalities and gender violence, housing and homelessness, migration and mobility, healthcare systems, and legal and policy environments.[21,39-45] Extreme inequities pervade the epidemiology of HIV and STIs. These determinants are interrelated and can influence each other, creating complex dynamics that contribute to the spread of HIV and STIs. Effective prevention, control, and elimination strategies require addressing these determinants comprehensively.

C OVID-19 and mental health

The COVID-19 pandemic, caused by the novel severe acute respiratory coronavirus 2 (SARS-CoV-2), has emerged as a global crisis of unprecedented magnitude since its initial outbreak in late 2019. According to WHO, COVID-19 has caused circa 7 million deaths, of which over 2 million have occurred in the WHO European Region.[46,47] The virus spreads primarily through respiratory droplets, leading to a wide range of symptoms, from mild flu-like symptoms to severe respiratory distress and even death.[48] Long COVID-19, a condition where individuals experience persistent symptoms or health issues that linger after initial recovery from SARS-CoV-2, has also created new challenges.[49] Since its initial outbreak, the virus has spread rapidly, affecting individuals, communities, and nations across the globe. The highly contagious nature of the virus led to the deployment of measures to limit its transmission, such as widespread testing, contact tracing, physical distancing, and the implementation of lockdowns and travel restrictions. The pandemic has resulted in significant health as well as social and economic consequences, challenging healthcare systems, disrupting daily life, and causing immense loss and hardship.

Healthcare systems worldwide have faced immense strain, with hospitals overwhelmed, medical supplies and resources stretched thin, and healthcare workers on the front lines facing unprecedented challenges.[50,51] The virus has caused a significant loss of life, with millions of individuals succumbing to the illness, leaving affected individuals and communities with distress and mourning. Furthermore, the pandemic has also affected the response to other diseases, halting or reserving global progress in other disease areas such as HIV, tuberculosis, and malaria.[52-54] For instance, the pandemic-related strain in healthcare systems along with physical distancing measures slowed down access to HIV and STIs testing and treatment services and interrupted prevention programmes.[54]

Beyond its health implications, the COVID-19 pandemic has had profound social and economic consequences.[55,56] Lockdowns and social distancing measures have resulted in widespread job losses, business closures, and economic downturns, as well as disruptions in the educational systems. Many individuals and communities have experienced financial hardship, food insecurity, and an increased risk of poverty[57,58]. The pandemic has also exposed and exacerbated existing societal inequalities.[59,60] Vulnerable populations, including the elderly, individuals with pre-existing health conditions, racial and ethnic minorities, and low-income communities, have been disproportionately affected by the virus.[59,60] Health disparities have been evident, with marginalized groups facing higher infection rates, worse health outcomes, and limited access to healthcare services.[56] Further, COVID-19 has exposed stark inequalities between countries globally, with disparities in access to healthcare, vaccination rates, economic resources, and infrastructure exacerbating the impact of the pandemic on different populations.[56-60]

Health impacts have not only occurred in terms of physical health but also on mental well-being, leading to increased rates of anxiety, depression, and other mental disorders.[61,62] Increased stress, fear, and isolation from the stringent measures, such as lockdowns, physical distancing, and quarantine, have disrupted daily routines, isolated individuals, and amplified feelings of uncertainty.[55,63] The COVID-19 pandemic has resulted in widespread job loss and increased poverty rates as businesses closed, industries struggled, and economies faced significant downturns, leaving many individuals and families facing financial hardships and an uncertain future.[57,59] The pandemic has also disrupted routine mental health services and limited access to care, exacerbating the existing mental health treatment gap.[61,62]

Studying the social, structural, and behavioural determinants of mental health during the COVID-19 pandemic is crucial because it allows us to understand the specific factors that influence mental well-being and identify vulnerable populations. It can also inform the development of targeted interventions and social protection measures to address the unique challenges posed by the pandemic, ultimately promoting resilience, equitable mental health support, and effective public health responses. These findings can also inform action for addressing the lingering mental health consequences of the COVID-19 pandemic and inform preparedness and response for future ones.

1.2 Aims and objectives

Aim:

The aim of this thesis is to investigate social, structural, and behavioural determinants of health by performing a series of studies on HIV, STIs, and mental health during the COVID-19 pandemic.

Objectives:

a) First objective

Investigate potential social, behavioural, and interventional determinants of rising syphilis rates among MSM in Europe, particularly examining the role of increased numbers of CAI sexual partners, more frequent screening, and PrEP use.

b) Second objective

Explore alternative designs of survey questions measuring the number of sexual partners by examining the clustering of reported numbers of sexual partners in studies with an open-answer format and providing an empirical basis for substituting categories with a range for partner numbers with their probable mean.

c) Third objective

Explore whether adopting antiretroviral therapy (ART) 'test-and-treat' guidelines (which recommend initiation of ART upon diagnosis regardless of CD4 cell count) improves population ART access and viral suppression, reducing overall HIV transmission rates.

d) Fourth objective

Examine the sociodemographic determinants of public stigma towards people with HIV and assess the relationship between stigma and HIV testing uptake.

e) Fifth objective

Examine associations between changes in mental health among older adults in Europe during the COVID-19 pandemic, socioeconomic characteristics, stringency of pandemic responses and social protection systems.

1.3 Peer-reviewed publications of the studies in this doctoral dissertation and contributions from the doctoral candidate

(chronological order)

1. Mendez-Lopez, A., White, T. M., Fuster-RuizdeApodaca, M.J., Lazarus, J. V. (2023) *Prevalence and sociodemographic determinants of public stigma towards people with HIV and its impact on HIV testing uptake: A cross-sectional study in 64 low- and middle-income countries.* ***HIV Medicine.*** doi: 10.1111/hiv.13536.

2. Mendez-Lopez, A., Stuckler, D., McKee, M., Semenza, J. C., & Lazarus, J. V. (2022). *The mental health crisis during the COVID-19 pandemic in older adults and the role of physical distancing interventions and social protection measures in 26 European countries.* ***SSM-Population Health***. doi: 10.1016/j.ssmph.2021.101017.

3. Mendez-Lopez, A., Stuckler, D., Marcus, U., Hickson, F., Noori, T., Whittaker, R. N., Jansen, K., Diaz, A., Henszel, L., Velter, A., Semenza, J. C.,* & Schmidt, A. J.* (2022) *Social and behavioural determinants of syphilis: Modelling based on repeated cross-sectional surveys from 2010 and 2017 among 278,256 men who have sex with men in 31 European countries.* **Lancet Regional Health Europe**. doi: 10.1016/j.lanepe.2022.100483.

4. Mendez-Lopez, A., Hickson, F., Jansen, K., Lachowsky, N., Burns. F, Folch, C., Velter, A., Weatherburn, P., Marcus, U., von Rüden. U., Mirandola, M., Gios, L., Frankis, J., Brennan, D. J., & Schmidt, A. J. (2022) *What is the empirical basis for converting banded ordinal data on numbers of sex partners among MSM into a continuous scale level variable? A secondary analysis of 13 surveys across 17 countries.* ***BMC Medical Research Methodology***. doi: 10.1186/s12874-021-01483-8.

5. Mendez-Lopez, A., McKee, M., Stuckler, D., Granich, R., Gupta, S., Noori, T., Semenza, J. C. (2019) *Population uptake and effectiveness of test-and-treat antiretroviral therapy guidelines for preventing the global spread of HIV: an ecological cross-national analysis.* ***HIV Medicine***. doi: 10.1111/hiv.12750.

Contributions:

In all the publications, the doctoral candidate, Ana Mendez-Lopez, was the lead author, contributing to the conceptualisation, research design, statistical analyses, data reporting in the text, tables and figures, and/or writing of the first draft and manuscript edits. As the lead author, the doctoral candidate coordinated all co-authors. She was also in charge of the management of all aspects of the submission of the manuscripts to indexed peer-reviewed journals, including updating the manuscripts based on reviewers' comments and responding to reviewers and editors.

1. 4 Funding, ethical considerations, and data access

The author declares no conflicts of interest.

No funding was received for the development of this thesis. Two of the included studies received funding for the data analysis and write-up from the European Centre for Disease Prevention and Control, which had no role in study design, data collection, data analysis, data interpretation, or writing of the report. This funding was not allocated to fund this thesis.

Data used are secondary data and no ethics approval was needed for any study. For studies 1, 2, 4, and 5, the data are publicly available in the duly cited data sources. Data can be accessed directly or upon registration and request. Data for study 3 may be accessed upon request to the data custodian (contact details can be found in the concerning publication).

1.5 References for the introduction

1. World Health Organization. A conceptual framework for action on the social determinants of health. 2010.

2. World Health Organization Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health: World Health Organization; 2008.

3. Marmot M. The health gap: the challenge of an unequal world. *The Lancet* 2015; **386**(10011): 2442-4.

4. World Health Organization. Social determinants of health: Key concepts. 2013. https://www.who.int/news-room/questions-and-answers/item/social-determinants-of-health-key-concepts.

5. World Health Organization. Social determinants of health: health topic. 2023. https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1.

6. Ramirez AG, Chalela P, Sabado-Liwag MD, Choi K. Behavioral Determinants in Population Health and Health Disparities Research. The Science of Health Disparities Research; 2021: 59-76.

7. World Health Organization. Sexually transmitted infections (STIs): Fact sheet. 2023. https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis) (accessed 14 June 2023).

8. World Health Organization. HIV and AIDS: Fact sheet. 2023. https://www.who.int/news-room/fact-sheets/detail/hiv-aids (accessed 14 June 2023).

9. Unemo M, Bradshaw CS, Hocking JS, et al. Sexually transmitted infections: challenges ahead. *Lancet Infect Dis* 2017; **17**(8): e235-e79.

10. Hook EW, 3rd. Syphilis. *The Lancet* 2017; **389**(10078): 1550-7.

11. World Health Organization. Syphilis: Health topics. 2023. https://www.who.int/health-topics/syphilis#tab=tab_1 (accessed 14 June 2023).

12. Maartens G, Celum C, Lewin SR. HIV infection: epidemiology, pathogenesis, treatment, and prevention. *Lancet* 2014; **384**(9939): 258-71.

13. Ghosn J, Taiwo B, Seedat S, Autran B, Katlama C. HIV. *Lancet* 2018; **392**(10148): 685-97.

14. UNAIDS. AIDSinfo. 2023. https://aidsinfo.unaids.org (accessed 14 June 2023).

15. WHO Regional Office for Europe, European Centre for Disease Prevention and Control. HIV/AIDS surveillance in Europe 2022 – 2021 data. Copenhagen: WHO Regional Office for Europe 2022.

16. World Health Organization. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. 2022.

17. World Health Organization. Global health sector strategy on sexually transmitted infections 2013-2020. Towards ending STIs. Geneva: World Health Organization, 2016.

18. Fu L, Sun Y, Han M, et al. Incidence Trends of Five Common Sexually Transmitted Infections Excluding HIV From 1990 to 2019 at the Global, Regional, and National Levels: Results From the Global Burden of Disease Study 2019. *Front Med (Lausanne)* 2022; **9**: 851635.

19. Peters RPH, Chico RM, Rowley J, Low N. Estimating the global burden of sexually transmitted infections. *The Lancet Infectious Diseases* 2022; **22**(8): 1112-3.

20. World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations: World Health Organization; 2016.

21. Nkengasong J, Ratevosian J. Legal and policy barriers for an effective HIV/AIDS response. *Lancet* 2023; **401**(10386): 1405-7.

22. UNAIDS. HIV and stigma and discrimination. Human rights Fact sheet series. Switzerland: UNAIDS, 2021.

23. Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. *J Int AIDS Soc* 2019; **22 Suppl 6**(Suppl Suppl 6): e25355.

24. World Health Organization. People who inject drugs - Global HIV, Hepatitis and STIs Programmes. 2023. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/populations/people-who-inject-drugs (accessed 24 September 2023.

25. Maxwell S, Shahmanesh M, Gafos M. Chemsex behaviours among men who have sex with men: A systematic review of the literature. *Int J Drug Policy* 2019; **63**: 74-89.

26. Newland J, Kelly-Hanku A. A qualitative scoping review of sexualised drug use (including Chemsex) of men who have sex with men and transgender women in Asia. *Retrieved from* 2021.

27. World Health Organization. Guide to starting and managing needle and syringe programmes. 2007.

28. World Health Organization. WHO/UNODC/UNAIDS position paper: Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention: World Health Organization; 2004.

29. Cepeda JA, Eritsyan K, Vickerman P, et al. Potential impact of implementing and scaling up harm reduction and antiretroviral therapy on HIV prevalence and mortality and overdose deaths among people who inject drugs in two Russian cities: a modelling study. *The Lancet HIV* 2018; **5**(10): e578-e87.

30. Heimer R. The Policy-Driven HIV Epidemic Among Opioid Users in the Russian Federation. *Curr HIV/AIDS Rep* 2018; **15**(3): 259-65.

31. Joint United Nations Programme on HIV/AIDS. Do no harm: health, human rights and people who use drugs: UNAIDS; 2016.

32. Lazarus JV, Wohl DA, Cascio M, et al. Long-term success for people living with HIV: A framework to guide practice. *HIV Med* 2023; **24 Suppl 2**: 8-19.

33. Lazarus JV, Safreed-Harmon K, Kamarulzaman A, et al. Consensus statement on the role of health systems in advancing the long-term well-being of people living with HIV. *Nat Commun* 2021; **12**(1): 4450.

34. Broderick K, Aristide C, Bullington BW, Mwanga-Amumpaire J, Downs JA, Sundararajan R. Stigma of infidelity associated with condom use explains low rates of condom uptake: qualitative data from Uganda and Tanzania. *Reproductive Health* 2023; **20**(1): 12.

35. Madiba S, Ngwenya N. Cultural practices, gender inequality and inconsistent condom use increase vulnerability to HIV infection: narratives from married and cohabiting women in rural communities in Mpumalanga province, South Africa. *Global health action* 2017; **10**(sup2): 1341597.

36. Reeves A, Steele S, Stuckler D, McKee M, Amato-Gauci A, Semenza JC. National sex work policy and HIV prevalence among sex workers: an ecological regression analysis of 27 European countries. *Lancet HIV* 2017; **4**(3): e134-e40.

37. Andersson GZ, Reinius M, Eriksson LE, et al. Stigma reduction interventions in people living with HIV to improve health-related quality of life. *Lancet HIV* 2020; **7**(2): e129-e40.

38. Mak WWS, Mo PKH, Ma GYK, Lam MYY. Meta-analysis and systematic review of studies on the effectiveness of HIV stigma reduction programs. *Social Science & Medicine* 2017; **188**: 30-40.

39. Sullivan PS, Johnson AS, Pembleton ES, et al. Epidemiology of HIV in the USA: epidemic burden, inequities, contexts, and responses. *The Lancet* 2021; **397**(10279): 1095-106.

40. Dean HD, Fenton KA. Addressing Social Determinants of Health in the Prevention and Control of HIV/AIDS, Viral Hepatitis, Sexually Transmitted Infections, and Tuberculosis. *Public Health Reports* 2010; **125**(4_suppl): 1-5.

41. Selvarajah S, Corona Maioli S, Deivanayagam TA, et al. Racism, xenophobia, and discrimination: mapping pathways to health outcomes. *The Lancet* 2022; **400**(10368): 2109-24.

42. Harling G, Subramanian SV, Barnighausen T, Kawachi I. Income inequality and sexually transmitted in the United States: who bears the burden? *Soc Sci Med* 2014; **102**: 174-82.

43. Baggaley RF, Zenner D, Bird P, et al. Prevention and treatment of infectious diseases in migrants in Europe in the era of universal health coverage. *The Lancet Public Health* 2022; **7**(10): e876-e84.

44. Kuchukhidze S, Panagiotoglou D, Boily M-C, et al. The effects of intimate partner violence on women's risk of HIV acquisition and engagement in the HIV treatment and care cascade: a pooled analysis of nationally representative surveys in sub-Saharan Africa. *The Lancet HIV* 2023; **10**(2): e107-e17.

45. Eiset AH, Wejse C. Review of infectious diseases in refugees and asylum seekers—current status and going forward. *Public Health Reviews* 2017; **38**(1): 22.

46. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. 2023 (accessed 14 June 2023).

47. World Health Organization Regional Office for Europe. Coronavirus disease (COVID-19) pandemic. 2023 (accessed 14 June 2023).

48. World Health Organization. Coronavirus disease (COVID-19): Health topics. 2023. https://www.who.int/health-topics/coronavirus#tab=tab_1 (accessed 14 June 2023).

49. Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol* 2023; **21**(3): 133-46.

50. World Health Organization. Pulse survey on continuity of essential health services during the COVID-19 pandemic: interim report, 27 August 2020: World Health Organization, 2020.

51. World Health Organization. Fourth round of the global pulse survey on continuity of essential health services during the COVID-19 pandemic: November 2022–January 2023: interim report, 1 May 2023: World Health Organization, 2023.

52. Global Fund. Results report 2021. 2021. https://www.theglobalfund.org/en/results/#downloadGeneva).

53. Global Fund. Results report 2022. 2022. https://www.theglobalfund.org/en/results/#downloadGeneva).

54. HIV Outcomes. The impact of COVID-19 on HIV in Europe. 2021. https://hivoutcomes.eu/wp-content/uploads/2022/02/220120-The-Impact-of-COVID-on-HIV-in-Europe.pdf (accessed 14 June 2023).

55. World Health Organization. Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March 2020: World Health Organization, 2020.

56. World Health Organization. Health inequity and the effects of COVID-19: assessing, responding to and mitigating the socioeconomic impact on health to build a better future: World Health Organization. Regional Office for Europe, 2020.

57. Bobrovnikova E, Gineikytė-Kanclerė V, Klimavičiūtė L, et al. Economic and social inequalities in Europe in the aftermath of the COVID-19 pandemic. 2023.

58. Mahler DG, Yonzan N, Lakner C. The impact of COVID-19 on global inequality and poverty. 2022.

59. Ferreira FH. Inequality: In the time of COVID-19 all metrics are not equal when it comes to assessing the pandemic's unequal effect. *Finance and Development* 2021: 20-3.

60. Sidik SM. How COVID has deepened inequality—in six stark graphics. *Nature* 2022; **606**(7915): 638-9.

61. World Health Organization. Mental health & COVID-19. 2023. https://www.who.int/teams/mental-health-and-substance-use/mental-health-and-covid-19 (accessed 14 June 2023).

62. World Health Organization. COVID-19 pandemic triggers 25% increase in prevalence of anxiety and depression worldwide. 2022 (accessed 14 June 2023).

63. United Nations Secretary-General Policy Brief. United Nations Policy Brief: COVID-19 and the need for action on mental health. *United Nations: New York, NY, USA* 2020.

2. Studies

2.1 Study 1: Social and behavioural determinants of syphilis: Modelling based on repeated cross-sectional surveys from 2010 and 2017 among 278,256 men who have sex with men in 31 European countries

Social and behavioural determinants of syphilis: Modelling based on repeated cross-sectional surveys from 2010 and 2017 among 278,256 men who have sex with men in 31 European countries

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Summary

Background Syphilis case notifications among men-who-have-sex-with-men (MSM) have increased markedly over the past two decades in Europe. We tested several potential factors for this resurgence.

Methods Self-reported data from two cross-sectional waves of the European MSM Internet Survey (EMIS-2010 and EMIS-2017, N = 278,256 participants living in 31 European countries) were used to fit multivariable hierarchical logistic regression models designed to evaluate potential social, behavioural, and interventional determinants of syphilis diagnosis. Additional multivariable hierarchical negative binomial models investigated determinants of the number of non-steady male condomless anal intercourse (CAI) partners. We tested the hypothesis that more CAI and syphilis-screening are associated with syphilis resurgence, both linked to use of pre-exposure prophylaxis (PrEP).

Findings Between 2010 and 2017, incidence of syphilis diagnosis in the previous 12 months rose from 2.33% (95%CI: 2.26−2.40) of respondents reporting a syphilis diagnosis in 2010 compared with 4.54% (95%CI: 4.42−4.66) in 2017. Major factors contributing to syphilis diagnosis were living with diagnosed HIV (adjusted odds ratio (aOR) 2.67, 95%CI: 2.32−3.07), each additional non-steady male CAI partner (aOR 1.01, 95%CI: 1.01−1.01), recency of STI-screening (previous month vs no screening, aOR 25.76, 95%CI: 18.23−36.41), selling sex (aOR 1.45, 95%CI: 1.27−1.65), and PrEP use (aOR 3.02, 95%CI: 2.30−3.96). Living with diagnosed HIV (adjusted incidence rate ratio (aIRR) 3.91, 95%CI: 3.77−4.05), selling sex (aIRR 4.39, 95%CI: 4.19−4.59), and PrEP use (aIRR 5.82, 95%CI: 5.29−6.41) were associated with a higher number of non-steady male CAI partners. The association between PrEP use and increased chance of syphilis diagnosis was mediated by STI-screening recency and number of non-steady male CAI partners, both substantially higher in 2017 compared to 2010.

Interpretation Syphilis cases are concentrated in three MSM population groups: HIV-diagnosed, PrEP users, and sex workers. Behavioural and interventional changes, particularly more non-steady male CAI partners and

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recency of STI-screening, are major contributing factors for increasing syphilis diagnoses among MSM in Europe.

Funding European Centre for Disease Prevention and Control.

Keywords: Men who have sex with men; MSM; Homosexual; Syphilis; Europe; STI-screening; Pre-exposure prophylaxis; PrEP; Condomless anal intercourse; Survey

Research in context

Evidence before this study

We searched PubMed for articles in any language between 1 January 2000 and 31 January 2022 using the following keywords and related terms in the title or abstract, or as MeSH terms, if existing: 'syphilis', 'men who have sex with men', and 'Europe', to identify individual studies and reviews. We additionally assessed surveillance data reports and found reports from the European Centre for Disease Prevention and Control showing increasing trends of syphilis case notifications to be concentrated in MSM. We found a recent systematic review and meta-analysis reporting pooled syphilis prevalence among MSM in Europe and North America in 2010-2020 was twice as high as in the previous decade 2000-2009, whereby the pooled prevalence has risen from 2.1% (95% CI: 0.8 to 3.9) in the period 2000-2009 to 4.2% (95% CI: 1.7 to 7.6) in 2010-2020. Another systematic review of syphilis trend studies in Western Europe and North America also reports increases in diagnoses since the year 2004. Several country-level studies show increases in syphilis case notifications, incidence or prevalence among MSM in different European countries. Some of these country studies assess determinants of syphilis diagnosis, including changes in sexual practices, sexual networks, and sexual healthcare contexts. Although there is evidence on the increasing trends of syphilis among MSM in Europe, there was limited direct evidence assessing simultaneously social, behavioural, and interventional determinants cross-nationally.

Added value of this study

This is the largest multi-country study documenting a higher rate of syphilis diagnoses between two time points (2010 and 2017) using data from repeated cross-sectional surveys among MSM in Europe along with the assessment of social, behavioural, and interventional determinants using harmonised survey data across countries. Incidence of syphilis in the MSM population has risen across Europe. Syphilis cases are concentrated in three MSM population groups: MSM diagnosed with HIV, MSM using PrEP, and MSM selling sex. The rise of syphilis diagnoses has disproportionately impacted HIV-diagnosed MSM and MSM sex workers. Major determinants are recency of last asymptomatic screening and number of non-steady condomless anal intercourse (CAI) male partners, both higher in 2017 compared to 2010, and both factors mediating the association between PrEP use and higher chance of syphilis diagnosis.

Implications of all the available evidence

MSM disclosing multiple CAI partners should be offered regular syphilis-screening due to their clearly increased risk and the serious possible sequelae of syphilis. Guidelines for the management of patients using PrEP include frequent syphilis-screening. Our finding that over a third of PrEP users were screened for STIs within the previous month provides support for the feasibility of implementing a regular HIV/STI-screening approach, such as the one in European guidelines for the management of PrEP users. Further, community-based education in MSM communities is needed to increase knowledge of and social norms for syphilis-screening. Efforts should be made to increase STI-screening in the MSM population, particularly among MSM sub-populations (HIV-diagnosed and sex workers) at high risk for syphilis, at least to match the sub-population with the highest screening rates (PrEP users).

Introduction

Syphilis is a curable sexually transmitted infection caused by *Treponema pallidum*, a motile Gram-negative spirochaete. Syphilis case notifications have risen markedly in many western European countries since record lows in 1998.[1–3] German surveillance data reveal a consistent increase in cases from 1955 in 2001 to 4077 in 2010, then to 7396 in 2020.[4] Similar patterns have been observed, among others, in England and Wales,[5] Scotland,[6] France,[7] and Norway.[8] A disproportionate burden of increasing syphilis diagnoses is occurring among MSM, of whom many have HIV co-infection.[1–3,9–12] This rise in syphilis is a sharp reversal of trends in the 1990s, when rates stabilized or declined in most European countries and the United States.[12]

The reasons for the resurgence of syphilis among MSM in Europe are not well understood. Increases in syphilis diagnoses in the United States and western Europe have been attributed to multiple behavioural factors, including changes in sexual practices (*e.g.*, increase in condomless anal intercourse (CAI), serosorting, the use of stimulant drugs before or during sex (chemsex), transactional sex, multiple (often anonymous) sexual partners), expansion of sexual networks (facilitated by technological developments such as the internet and geospatial apps for finding partners), and changes in sexual healthcare contexts (*e.g.*, increased care-seeking behaviour through uptake of STI-screening and use of chemotherapies).[3,11–18] Hypothesised drivers for these changes include elimination of HIV infectivity in HIV positive men on treatment and elimination of HIV susceptibility through chemoprophylaxis (in particular PrEP) in HIV-negative men.[12,19,20]

Further, rising syphilis rates have not been curbed, in part, due to the insufficient scale of prevention services as part of syphilis programmes, including better performance in active case-finding and curing cases, healthcare workers awareness, laboratory capacity and healthcare infrastructure, and funding.[12,19] Coverage of preventive healthcare services has been particularly problematic in populations with high incidence of STI such as MSM, for whom coverage of services such as case finding may be particularly problematic as stigmatised sexual minority and sexual settings with a high degree of anonymity.

Syphilis is a notifiable disease in all EU/EFTA countries, with reliable surveillance data based on laboratory-confirmed diagnosis. However, gaps exist in the surveillance of syphilis in the MSM population. For example, syphilis surveillance data in some EU countries are not disaggregated by gender of sexual partners,[21] making it difficult to compare trends across countries and over time. The European MSM Internet Survey (EMIS) is a community-recruited, self-selecting, self-reporting online cross-sectional survey for MSM. It combines epidemiological, psychosocial, behavioural, and interventional data, and is the largest dataset of this type across European countries. Surveys were conducted in 2010 and 2017.[22–25] Using EMIS data, we examined some potential determinants of rising syphilis rates among MSM in this study period. We investigated social, behavioural, and interventional factors linked to the MSM syphilis epidemic, testing the hypothesis that an increase in CAI with non-steady partners is associated with syphilis resurgence, and examining factors that may be associated with the number of CAI partners, including HIV PrEP use and associated more frequent screening detecting more syphilis cases.[26]

Methods

Source of data

Details of the EMIS survey have been described elsewhere.[24,25] Briefly, a non-probability sample of participants was recruited through direct-to-user invitations in online-dating platforms, geo-spatial dating apps (2017 only), and social media channels, and ads on websites of EMIS civil society partners (more details in Appendix 1 and on the project's website: www.emis2017.eu). EMIS-2010 was available online for completion for 12 weeks, between 4 June and 31 August 2010.[22] Online promotion of EMIS-2017 began on 18 October 2017 and ran until 31 January 2018.[23] For these analyses we included respondents from 30 European countries that as of 2017 were part of the European Centre for Disease Prevention and Control mandate on disease surveillance. We also included respondents from Switzerland and four European microstates (Andorra, Monaco, San Marino, and Liechtenstein, all of which are included in the samples of neighbouring countries). Hence in this publication we refer to 31 European countries, while technically respondents from 35 countries are included in the study sample.

Main outcome measure

Syphilis diagnosis was self-reported. Participants were asked if they had ever been diagnosed with syphilis and, if so, when they had last been diagnosed (within 24 hours, last 7 days, 4 weeks, 6 months, 12 months, 5 years, or longer ago). We constructed the incidence of syphilis diagnosis based on self-reported diagnosis within the previous 12 months.

Respondents using the French version of the 2017 questionnaire were likely to over-report syphilis diagnoses because of sub-optimal translation of questions on STI diagnoses (details in Appendix 1).[23] All statistical models are adjusted for potential bias arising from this issue.

Exposure variables

We assessed five sociodemographic variables as determinants of syphilis diagnosis and number of non-steady male CAI partners, including age (and age squared to account for potential non-linear effects of age during the life course), educational level, occupational status, settlement size, and whether the respondent was born in the country of residence.

To capture risky sexual behaviour with respect to syphilis transmission, we assessed the number of male sexual partners by type and sexual act within the previous 12 months, differentiating whether partners were steady or non-steady, and whether the sexual act included condomless anal intercourse (CAI).[27] Additional behavioural risk factors are whether the respondent engaged in transactional sex, including paying for sex and selling sex during the previous 12 months.

We assessed care-seeking behaviour for STI-screening (other than HIV) as the recency of last screening. Thus, between survey waves, recency of the last STI-screening is a marker for behavioural/interventional change. Additionally, recency of screening is a marker of uptake of and adherence to PrEP guidelines, thus, being a factor affecting the likelihood of diagnosing syphilis, particularly recent and asymptomatic infections. STI-screening almost universally featured a blood test in both waves.[26]

We also assessed HIV-serosorting (whether the respondent had CAI only with males with the same HIV diagnosis as himself), knowledge that an undetectable HIV viral load equals untransmissibility (U=U), HIV diagnosis, and whether the respondent used PrEP daily or on demand or not. PrEP was not established/available in 2010 and thus captured only in the 2017 wave. Analyses involving this variable are restricted to data for only the second wave.

Finally, we accounted for the potential role of respondents' survey recruitment source, differentiating between recruitment via dating apps, social media, or unknown (Supplemental data: Appendix 1).

Statistical analyses

First, we report estimates of incidence of self-reported syphilis diagnosis within the previous 12 months in 31 European countries for the years 2010 and 2017, estimating the overall change between survey waves adjusted for whether the language of the questionnaire was French.

Second, individual-level multivariable hierarchical logistic regression models (generalized linear models with logit-link function and binomial distribution) with country random intercepts were used to examine associations with the odds of syphilis diagnosis. Next, we ran additional individual-level multivariable hierarchical negative binomial models (generalized linear model with log-link and negative binomial distribution) with country random intercepts to estimate determinants of the incidence rate for the number non-steady male CAI partners. Finally, subsequent hierarchical negative binomial and logistic regression models with country random intercepts examine, respectively, the association of PrEP use with the incidence rate of the number of non-steady male CAI partners and odds of syphilis diagnosis, testing for mediation of number of non-steady male CAI partners and recency of last STI-screening, as proxy of disease detection through testing frequency, in the association between PrEP use and the outcome measure in 2017. Estimates from regression models were used to compute marginal mean probabilities of syphilis diagnosis and mean number of non-steady male CAI partners.

In further models we assessed robustness to model specification. We report robust standard errors clustered by country. Missing data were handled with pairwise deletion. Analyses were performed using Stata 16.0.[28]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The lead author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The final analytic sample, after excluding cases with missing answers to the main outcome measure, included 166,426 (2010 wave) and 111,830 (2017 wave) people identifying as men who have sex with men and/or being sexually attracted to men (N = 278,256).

Change in the incidence of syphilis diagnosis

In 2010, 3875 (2.33%, 95%CI: 2.26−2.40) respondents reported a syphilis diagnosis in the previous 12 months compared with 5074 (4.54%, 95%CI: 4.42−4.66) in 2017 (Figure 1 and Table 1), a difference of 2.21 percentage points (ppt) (95% confidence interval (CI): 2.08 −2.34), which dropped to 1.37ppt (95%CI: 1.12−1.62) after adjusting for French language questionnaire and country fixed effects (Supplemental data: Appendix 2).

Figure 1 plots the estimated incidence for the previous 12 months by country. Portugal (3.39%, 95%CI: 2.41−4.38), Bulgaria (2.42%, 95%CI: 1.13−3.71), and Malta (2.32%, 95%CI: 1.03−5.68) had the largest estimated difference in reported incidence between 2010 and 2017 (excluding the countries with high proportions of respondents using the French questionnaire), whereas Sweden (0.59%, 95%CI: 0.14−1.04), Denmark (0.22%, 95%CI: 0.92−1.36) and Croatia (0.15%, 95%CI: 0.92−1.22) had the smallest. Only Luxembourg had a lower proportion of respondents reporting a syphilis diagnosis in 2017 compared with 2010, although not statistically significant (-1.02%, 95%CI: -4.04 −2.00).

Determinants of syphilis diagnosis

The odds of syphilis diagnosis in the previous 12 months increased with age (aOR 1.05 per year of age, 95%CI: 1.03−1.07) (Table 2). We found a dose-response relationship in the association between the odds of syphilis diagnosis and educational level, whereby a higher educational level was associated with lower odds (aOR high vs low level: 0.64, 95%CI: 0.56−0.72; aOR medium vs low level: 0.79, 95%CI: 0.70−0.91).

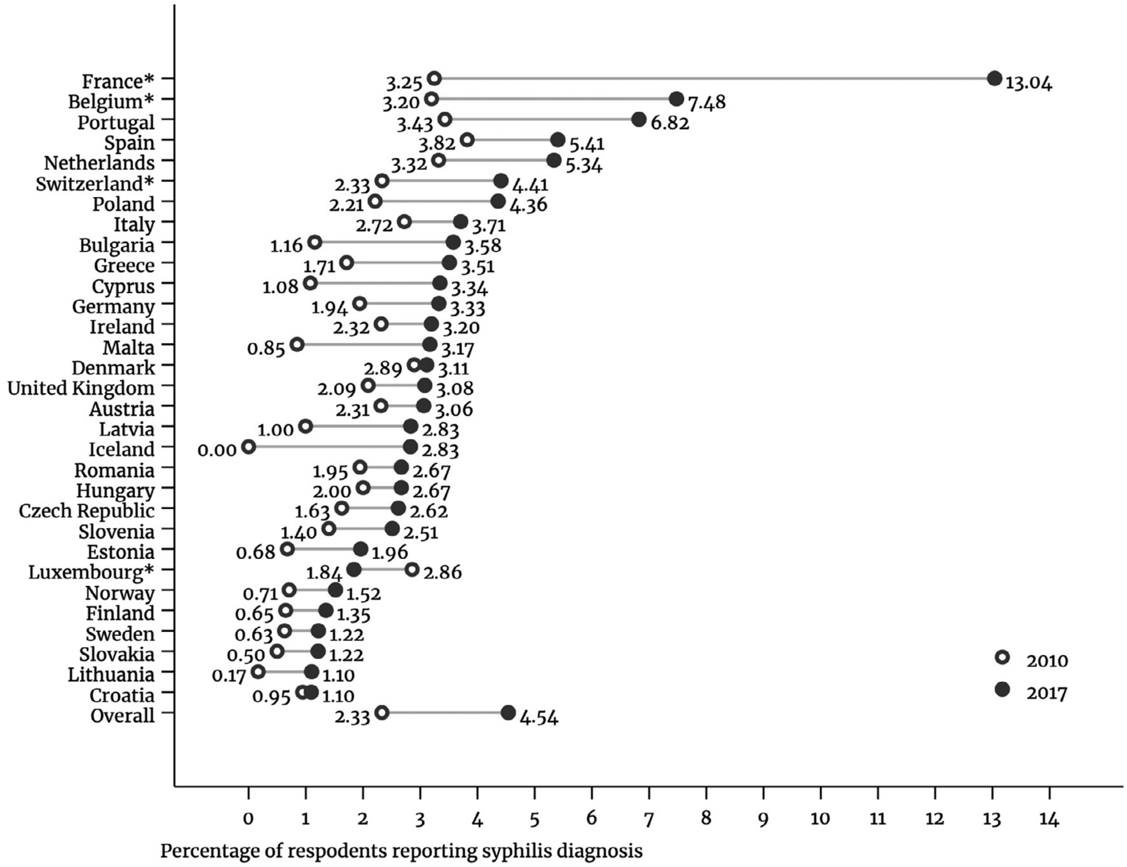

Figure 1. Incidence of self-reported syphilis diagnosis within the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.

* Country with a high proportion of respondents using the French version of the questionnaire likely to have inflated the total number of affirmative responses to syphilis diagnoses in 2017 because of how the question was asked (sub-optimal translation); percentage does not exclude responses from those who used the French questionnaire.

Compared to employed individuals, unemployed individuals had higher odds of diagnosis (aOR 1.12, 95%CI: 1.04–1.20), while students (aOR 0.75, 95%CI: 0.70–0.81) and individuals retired, on long-term sick leave or other (aOR 0.86, 95%CI: 0.77–0.97) had lower odds of syphilis diagnosis. No difference in odds was found between individuals living in different size settlements (aOR 0.94, 95%CI: 0.85–1.04). Individuals born abroad their country of residence were 1.22 times more likely of being diagnosed with syphilis (95%CI: 1.10–1.36).

Living with diagnosed HIV was associated with higher odds of syphilis diagnosis (aOR 2.67, 95%CI: 2.32–3.07) (Table 2), which accounted for a 5.46% marginal mean probability of syphilis diagnosis among individuals living with diagnosed HIV and 2.46% probability among individuals not living with diagnosed with HIV (Figure 2). Across survey waves, the proportion of respondents living with HIV reporting a syphilis diagnosis (13.82%, 95%CI: 13.39–14.25) was more than six-fold that of respondents not living with HIV (2.17%, 95%CI: 2.12–2.23) (estimates not shown in tables), raising from 11.79% (95%CI: 11.23–12.33) in 2010 to 16.15% (95%CI: 15.48–16.82) in 2017 among HIV-diagnosed respondents (Figure 3 and Table 3).

We observed a dose-response relationship whereby the odds of being diagnosed with syphilis were higher for those who had screened more recently. Compared to those who had not screened within the previous 12 months, the odds ratios of syphilis diagnosis were 25.77 (95%CI: 18.23–36.41), 16.06 (95%CI: 11.63–22.18) and 7.25 (95%CI: 5.37–9.78) for those who had screened asymptomatically within the previous month, 2–6 months, and 7–12 months, respectively (Table 2). For those who had a symptomatic STI test performed, the odds ratio of being diagnosed with syphilis, compared to those who did not screen at all, was 74.82 (95%CI: 51.44–108.81). These estimates accounted for a probability of syphilis diagnosis of 6.10% (95%CI: 5.38–6.82), 3.98% (95%CI: 3.38–), and 1.88% (95%CI: 1.24–2.52) for those who had screened asymptomatically

	N	Mean (SD) or proportion	N	Mean (SD) or Proportion
	2010		2017	
Sample size[a]	166,426	100%	111,830	100%
Syphilis diagnosis previous 12 months				
No	162,551	97.67%	106,756	95.46%
Yes	3875	2.33%	5074	4.54%
Age	166,426	34.34 (11.37)	111,830	37.99 (12.95)
Educational level				
Low	13,987	8.45%	5220	5.02%
Mid at least upper secondary; 2–5 years post 16	71,197	43.02%	37,725	36.31%
High first stage of tertiary or more; 6+ years post 16	80,331	48.53%	60,955	58.67%
Occupational status				
Employed (full/part/self)	117,903	71.14%	80,734	72.39%
Unemployed	10,062	6.07%	5977	5.36%
Student	25,752	15.54%	15,648	14.03%
Retired, long-term sick leave, other	12,018	7.25%	9163	8.22%
Settlement size				
Village/small town <100,000 inhabitants	55,529	34.19%	38,785	35.07%
Big/medium town ≥100,000 inhabitants	106,884	65.81%	71,807	64.93%
Country of birth				
Born in country of residence	140,666	86.66%	96,320	86.24%
Born abroad	21,662	13.34%	15,366	13.76%
HIV diagnosis				
No	152,364	92.05%	99,605	89.64%
Yes	13,158	7.95%	11,511	10.36%
STI-screening				
No STI-screening previous 12 months	106,020	67.80%	58,743	54.59%
Last STI-screening during previous month	7032	4.50%	9194	8.54%
Last STI-screening 2–6 months ago	18,242	11.67%	19,696	18.30%
Last STI-screening 7–12 months ago	13,658	8.73%	10,731	9.97%
Symptomatic STI test during previous 12 months	11,415	7.30%	9244	8.59%
Number of steady male sexual partners in the previous 12 months	165,287	1.82 (5.95)	110,868	1.59 (5.53)
Number of non-steady male sexual partners in the previous 12 months	164,538	11.25 (25.04)	110,136	12.69 (26.56)
Number of condomless intercourse steady male partners in the previous 12 months	164,183	0.68 (2.95)	108,596	0.83 (3.73)
Number of condomless non-steady male partners in the previous 12 months	162,562	1.75 (9.86)	107,231	3.73 (14.93)
Paid for sex in the previous 12 months				
No	153,249	92.81%	101,590	90.88%
Yes	11,873	7.19%	10,200	9.12%
Sold sex in the previous 12 months				
No	157,356	95.24%	107,000	95.75%
Yes	7867	4.76%	4752	4.25%
Serosorting in the previous 12 months[c]				
No	126,104	92.04%	88,798	90.45%
Yes	10,902	7.96%	9379	9.55%
Knowledge of U=U				
I didn't know/understand/believe/wasn't sure	82,806	49.90%	45,762	41.02%
I knew this already	83,151	50.10%	65,809	58.98%
PrEP use[b]				
Not currently taking PrEP	-	-	96,305	96.71%
Currently taking PrEP daily or on demand	-	-	3281	3.29%

***Table 1*: Summary statistics in 31 European countries[a], European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.**

[a] Some countries include the responses of neighbouring smaller states with low number of respondents. List of microstates (with name of larger state with which their data is merged in brackets): Monaco (France), San Marino (Italy), Andorra (Spain), and Liechtenstein (Switzerland).

[b] Remaining number of participants are HIV-diagnosed individuals not eligible for PrEP use.

[c] Non-steady male CAI partners based on HIV-serosorting in the previous 12 months.

	Syphilis diagnosis	
	Adjusted odds ratio	**95% confidence interval**
Year		
2010	reference	
2017	1.181**	1.062 to 1.313
Questionnaire language		
Other than French	reference	
French	2.837***	2.374 to 3.390
Age	1.051***	1.033 to 1.070
Age squared	0.999***	0.999 to 0.999
Educational level		
Low	reference	
Mid at least upper secondary; 2–5 years post 16	0.794***	0.695 to 0.907
High first stage of tertiary or more; 6+ years post 16	0.635***	0.561 to 0.719
Occupational status		
Employed full/part/self	reference	
Unemployed	1.117**	1.039 to 1.201
Student	0.751***	0.695 to 0.812
Retired/Long-term sick leave/Other	0.863*	0.772 to 0.966
Settlement size		
Small town/village <100,000 inhabitants.	reference	
Medium/big town ≥100,000 inhabitants	0.940	0.848 to 1.043
Country of birth		
Born in country of residence	reference	
Born abroad	1.221***	1.099 to 1.357
Diagnosed with HIV		
No	reference	
Yes	2.669***	2.321 to 3.068
Recency of last screening or testing		
No STI-screening previous 12 months	reference	
Last STI-screening during previous month	25.767***	18.233 to 36.414
Last STI-screening 2–6 months ago	16.061***	11.630 to 22.180
Last STI-screening 7–12 months ago	7.250***	5.372 to 9.784
Symptomatic STI test during previous 12 months	74.815***	51.443 to 108.807
Number of steady male sexual partners in the previous 12 months	1.006*	1.001 to 1.011
Number of non-steady male sexual partners in the previous 12 months	1.004***	1.002 to 1.005
Number of steady male CAI partners in the previous 12 months	1.006	0.999 to 1.013
Number of non-steady male CAI partners in the previous 12 months	1.008***	1.007 to 1.009
Paid for sex in the previous 12 months		
No	reference	
Yes	1.223***	1.121 to 1.335
Sold sex in the previous 12 months		
No	reference	
Yes	1.446***	1.267 to 1.650
Survey recruitment source		
Dating apps (Romeo, Grindr, Hornet, other dating apps/websites)	reference	
Social media (Facebook, Twitter, Instagram, other)	0.814***	0.740 to 0.895
Unknown tracking code	0.909	0.770 to 1.073
Country random intercepts	1.141**	1.053 to 1.236
Number of individuals	234719	

***Table 2*: Determinants of change in the odds of reporting a syphilis diagnosis within the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.**

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; robust standard errors adjusted by country; CAI, condomless anal intercourse.

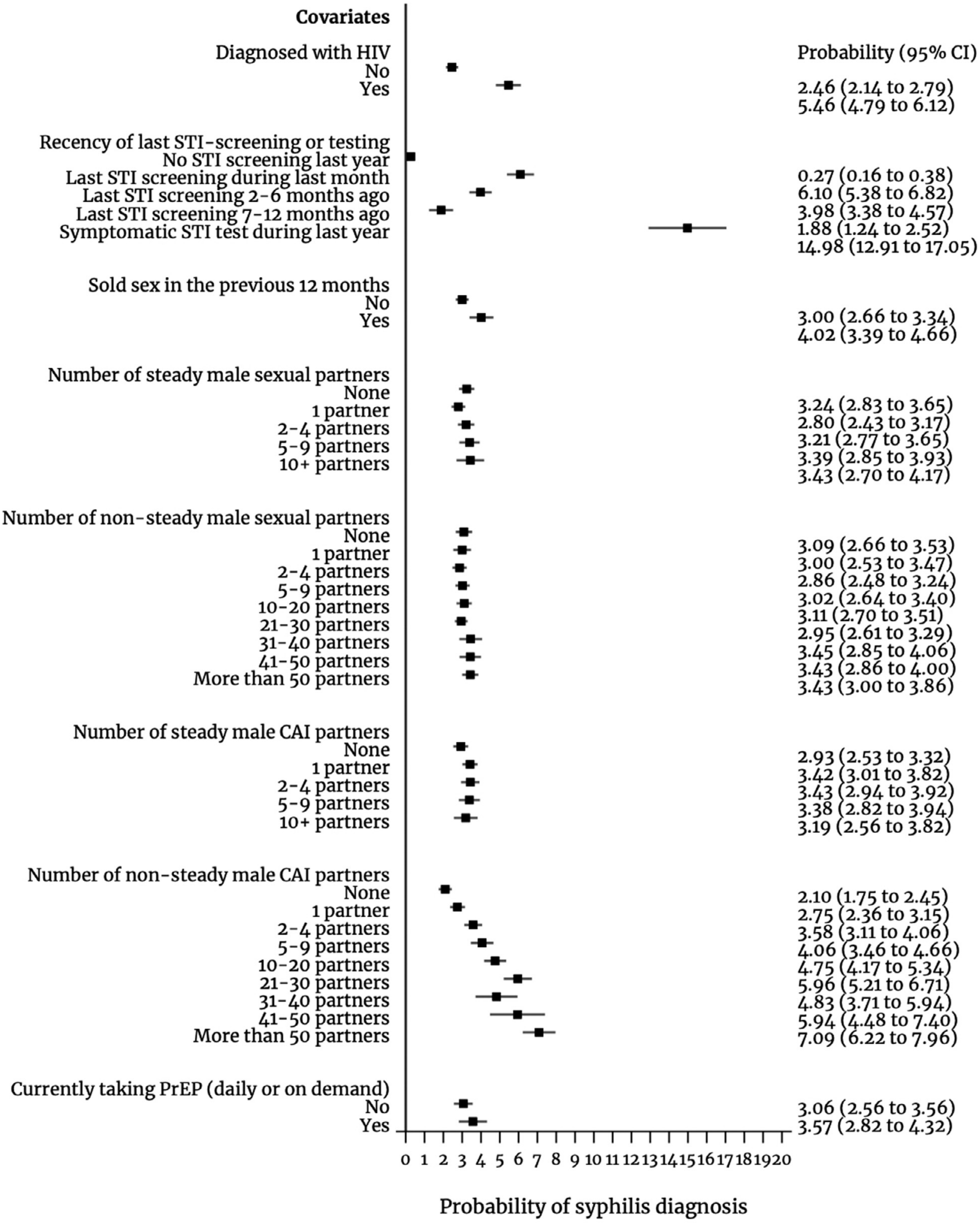

Figure 2. Predicted probability of syphilis diagnosis for selected covariates (marginal predicted mean probability) in 31 countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.

CAI: condomless anal intercourse. Results for covariate measuring PrEP use are only for the year 2017 and the estimates for this covariate are based on a sample size of only 30 countries as in one country (Latvia) there were no PrEP users.

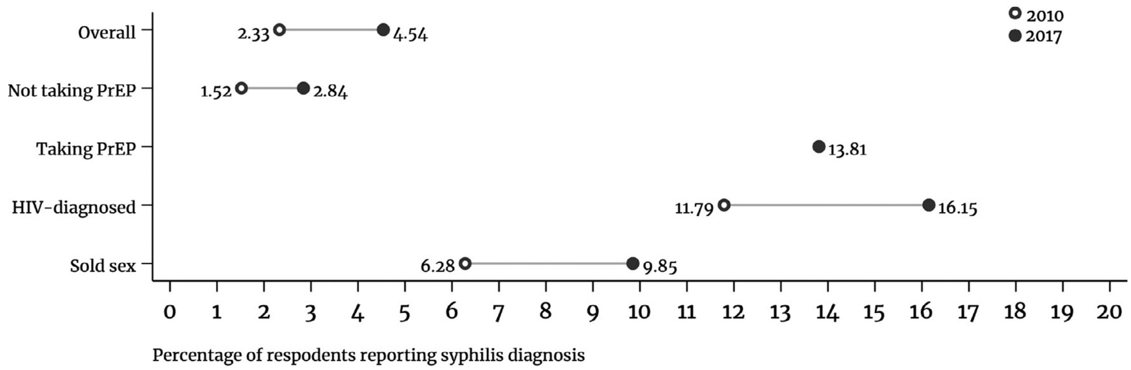

Figure 3. Incidence of self-reported syphilis diagnosis within the previous 12 months overall and in key population groups across 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.

Note: 'Not taking PrEP' sample in 2010 includes the overall sample except for individuals diagnosed with HIV who would have not been eligible for PrEP. In 2017, 'not taking PrEP' sample includes the overall sample except for individuals diagnosed with HIV who are not eligible for PrEP and individuals taking PrEP.

within the previous month, 2–6 months, and 7–12 months, respectively (Figure 2). Those who during the last year had performed a symptomatic STI test had a 14.98% probability of being diagnosed with syphilis. This probability was 0.27% (95%CI: 0.16–0.38) for individuals not screened during the last year. Screening for STI increased between survey waves, particularly among those reporting their last screen was within the previous month (raising from 4.50% (95%CI: 4.40–4.61) in 2010 to 8.54% (95%CI: 8.38–8.71) in 2017) and within the previous 2–6 months (from 11.67% (95%CI: 11.45–11.78) in 2010 to 18.30% (95%CI: 18.03–18.48) in 2017) (Table 1 and Table 3).

Each additional steady male sexual partner (aOR 1.006, 95%CI: 1.001–1.011), non-steady male sexual partner (aOR 1.004, 95%CI: 1.002–1.015), CAI steady male partner (aOR 1.006, 95%CI: 1.001–1.011) and CAI non-steady male partner (aOR 1.008, 95%CI: 1.007–1.009) were associated, on average, with a higher odds of syphilis diagnosis (in more detailed decimal numbers) (Table 2). Figure 2 depicts the association between disaggregated numbers of different types of male sexual partners (using ordinal variables instead of continuous variables as above) with the marginal mean probability of syphilis diagnosis. We observed a substantial increased probability with the CAI non-steady male partners measure (for instance, 3.43% probability of syphilis diagnosis for those reporting more than 50 non-steady male partners vs 7.09% for those reporting more than 50 non-steady male CAI partners), with a strong dose-response relationship, whereby greater numbers of partners were linked to a higher probability of syphilis diagnosis. The mean number of male partners was higher in 2017 compared to 2010, particularly non-steady CAI partners, which more than doubled (Table 1), with doubling numbers occurring among those reporting more than 5 and up to more than 50 non-steady CAI partners (Table 3). The proportion of individuals reporting more than 50 non-steady male CAI partners raised from 0.52% (95%CI: 0.48–0.54) in 2010 to 1.20% (95%CI: 1.14–1.27) in 2017 (Table 3).

Engagement in transactional sex increased the odds of syphilis diagnosis, less among people buying sex (aOR 1.22, 95%CI: 1.21–1.34) than among those selling sex (aOR 1.45, 95%CI: 1.27–1.65) (Table 2); for the latter the marginal probability of syphilis diagnosis was 4.02% (95%CI: 3.39–4.66) vs 3.00% (95%CI: 2.66–3.34) among those not selling sex (Figure 2). Across survey waves, the proportion of syphilis diagnoses among people selling sex (7.62%, 95%CI: 7.16–8.09) was 2.5 times greater than among those who did not (3.01%, 95%CI: 2.94–3.07), increasing from 6.28% (95%CI: 5.74–6.82) in 2010 to 9.85% (95%CI: 9.00–10.70) in 2017 among people selling sex (Figure 3 and Table 3).

Finally, Table 2 shows, first, that respondents of the French questionnaire in 2017 had a higher odds of reporting a syphilis diagnosis (aOR 2.84, 95%CI: 2.37–3.39). Second, individuals recruited via social media had lower odds of syphilis diagnosis compared to individuals recruited via dating apps (aOR 0.81, 95%CI: 0.74–0.90).

Determinants of the number of non-steady male CAI partners

In 2017, the incidence rate for the count of non-steady male CAI partners was 1.71 (95%CI: 1.67–1.74) times the rate in 2010, after adjusting for multiple potential determinants (Table 4). The expected number of non-steady male CAI partners decreased with educational level in a dose-response relationship (aIRR for high vs low educational level: 0.75, 95%CI: 0.72–0.78; aIRR for mid vs low educational level: 0.88, 95%CI: 0.84–0.92). Compared to employed individuals, unemployed individuals had a higher expected count of non-steady male

	2010								2017									
	Overall		Not taking PrEP[a]		Not eligible for PrEP: HIV+		Sold sex		Overall		Not taking PrEP[b]		Not eligible for PrEP: HIV+		Taking PrEP[c]		Sold sex	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Syphilis diagnosis																		
Yes	3875	2.33	2324	1.52	1551	11.79	494	6.28	5074	4.54	2739	2.84	1859	16.15	453	13.81	468	9.85
No	162,551	97.67	150,944	98.48	11,607	88.21	7373	93.72	106,756	95.46	93,566	97.16	9652	83.85	2828	86.19	4284	90.15
Number of non-steady male CAI partners																		
None	118,334	72.79	112,552	75.12	5782	45.39	3541	46.35	64,557	60.20	60,126	65.00	3472	31.75	472	15.28	1436	31.88
1	18,760	11.54	17,619	11.76	1141	8.96	1056	13.82	13,451	12.54	12,224	13.21	929	8.49	213	6.89	563	12.5
2–4	15,831	9.74	13,807	9.22	2024	15.89	1505	19.7	15,434	14.39	12,874	13.92	1888	17.26	593	19.19	1015	22.53
5–-9	3982	2.45	2913	1.94	1069	8.39	498	6.52	5257	4.90	3599	3.89	1174	10.74	459	14.85	436	9.68
10–20	3423	2.11	2050	1.37	1373	10.78	537	7.03	4944	4.61	2551	2.76	1706	15.60	670	21.68	483	10.72
21–30	779	0.48	350	0.23	429	3.37	144	1.88	1371	1.28	503	0.54	610	5.58	256	8.28	172	3.82
31–40	395	0.24	166	0.11	229	1.8	79	1.03	573	0.53	183	0.20	286	2.62	103	3.33	88	1.95
41–50	232	0.14	74	0.05	158	1.24	60	0.79	353	0.33	114	0.12	171	1.56	68	2.20	71	1.58
> 50	826	0.51	293	0.20	533	4.18	220	2.88	1291	1.20	330	0.36	700	6.40	256	8.28	241	5.35
Recency of last STI-screening previous 12 months																		
No STI-screening	106,020	67.80	102,726	71.41	3294	26.32	3954	53.75	58,743	54.59	55,715	60.15	2349	21.16	251	7.80	1908	41.77
During previous month	7032	4.50	4980	3.46	2052	16.39	591	8.03	9194	8.54	5763	6.22	2151	19.38	1242	38.60	600	13.13
2–6 months ago	18,242	11.67	14,586	10.14	3656	29.21	1182	16.07	19,696	18.30	14,715	15.89	3795	34.19	1098	34.12	996	21.80
7–12 months ago	13,658	8.73	12,131	8.43	1527	12.2	655	8.90	10,731	9.97	9474	10.23	1088	9.80	104	3.23	370	8.10
Symptomatic STI test	11,415	7.30	9427	6.55	1988	15.88	974	13.24	9244	8.59	6962	7.52	1718	15.48	523	16.25	694	15.19

***Table 3*: Syphilis diagnosis in the previous 12 months, number of non-steady male CAI partners, and recency of last STI-screening, overall and in key population groups by survey wave (2010 and 2017) in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.**

[a] Overall sample excluding individuals diagnosed with HIV.

[b] Overall sample excluding individuals diagnosed with HIV and individuals taking PrEP daily or on demand.

[c] Taking PrEP daily or on demand.

	Number of non-steady male CAI partners	
	Adjusted incidence rate ratio	**95% confidence interval**
Year		
2010	reference	
2017	1.705***	1.667 to 1.743
Age	1.047***	1.041 to 1.053
Age squared	1.000***	0.999 to 1.000
Educational level		
Low	reference	
Mid at least upper secondary; 2—5 years post 16	0.881***	0.844 to 0.920
High first stage of tertiary or more; 6+ years post 16	0.746***	0.715 to 0.779
Occupational status		
Employed full/part/self	1.000	
Unemployed	1.167***	1.117 to 1.219
Student	0.730***	0.704 to 0.757
Retired/Long-term sick leave/Other	1.018	0.975 to 1.063
Settlement size		
Small town/village <100,000 inhabitants	reference	1.000 to 1.000
Medium/big town ≥100,000 inhabitants	1.089***	1.064 to 1.114
Country of birth		
Born in country of residence	reference	
Born abroad	1.178***	1.143 to 1.214
Diagnosed with HIV		
No	reference	
Yes	3.905***	3.771 to 4.045
Recency of last STI-screening or testing		
No STI-screening previous 12 months	reference	
Last STI-screening during previous month	3.041***	2.915 to 3.172
Last STI-screening 2—6 months ago	2.014***	1.953 to 2.077
Last STI-screening 7—12 months ago	1.274***	1.228 to 1.321
Symptomatic STI test during previous 12 months	3.263***	3.143 to 3.387
Paid for sex in the previous 12 months		
No	reference	
Yes	1.496***	1.443 to 1.552
Sold sex in the previous 12 months		
No	reference	
Yes	4.388***	4.193 to 4.593
Knowledge about HIV undetectable equals untransmissible (U=U)		
I didn't know/understand/believe/wasn't sure	1.000	
I knew this already	1.625***	1.590 to 1.661
CAI partners based on HIV-serosorting in the previous 12 months		
No	reference	
Yes	1.686***	1.627 to 1.747
Survey recruitment source		
Dating apps (Romeo, Grindr, Hornet, other dating apps/websites)	reference	
Social media (Facebook, Twitter, Instagram, other)	0.868***	0.843 to 0.894
Unknown tracking code	0.822***	0.764 to 0.885
Log-transformed overdispersion parameter	4.672***	4.627 to 4.718
Country random intercepts	1.028**	1.011 to 1.045
Number of individuals	203467	

***Table 4*: Determinants of change in the incidence rate of reporting a number non-steady CAI partners within the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.**

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; Robust standard errors adjusted by country; CAI, condomless anal intercourse.

CAI partners (aIRR 1.17, 95%CI: 1.12–1.22) yet students had a lower expected count (aIRR 0.73, 95%CI: 0.70–0.76). No difference was observed between unemployed individuals and those retired, in long-term sick leave or other (aIRR 1.02, 95%CI: 0.98–1.06). The incidence rate was higher for individuals living in settlements of bigger size (aIRR 1.09, 95%CI: 1.06–1.11) and for individuals born outside the country of residence (aIRR 1.18, 95%CI: 1.14–1.21). Survey participants recruited through social media (aIRR 0.87, 95%CI: 0.84–0.89) or with unknown recruitment (aIRR 0.82, 95%CI: 0.76–0.89) had a lower expected count of non-steady male CAI partners than respondents recruited through dating apps.

We observed the greatest impact on the number of non-steady male CAI partners to be associated with HIV diagnosis and behavioural and interventional factors. We found men with diagnosed HIV had an incidence rate for the number of non-steady male CAI partners 3.91 (95%CI: 3.77–4.05) times that of those without diagnosed HIV (Table 4). The marginal predicted number of non-steady male CAI partners was 7.75 (95%CI: 6.76–8.75) among people living with diagnosed HIV vs 1.99 (95%CI: 1.82–2.15) among those not diagnosed with HIV (Figure 4). We estimated the reported number of non-steady CAI partners among people living with HIV rose from 10.16 (95%CI: 9.71–10.62) in 2010 to 14.96 (95%CI: 14.38–15.55) in 2017 (results not in tables, disaggregated by bands in Table 3).

More recent STI-screening was also associated with a higher number of non-steady male CAI partners: compared with no screening in the previous 12 months, the incidence rate for the count of non-steady male CAI partners was 3.04 (95%CI: 2.92–1.72), 2.01 (95%CI: 1.95–2.08), and 1.27 (95%CI: 1.23–1.32) times, respectively, for those who had screened asymptomatically within the previous month, 2–6 months, and 7–12 months (Table 4). For these, the predicted mean number of non-steady male CAI partners were 5.20 (95%CI: 4.39–6.01), 3.44 (95%CI: 3.04–3.85), and 2.18

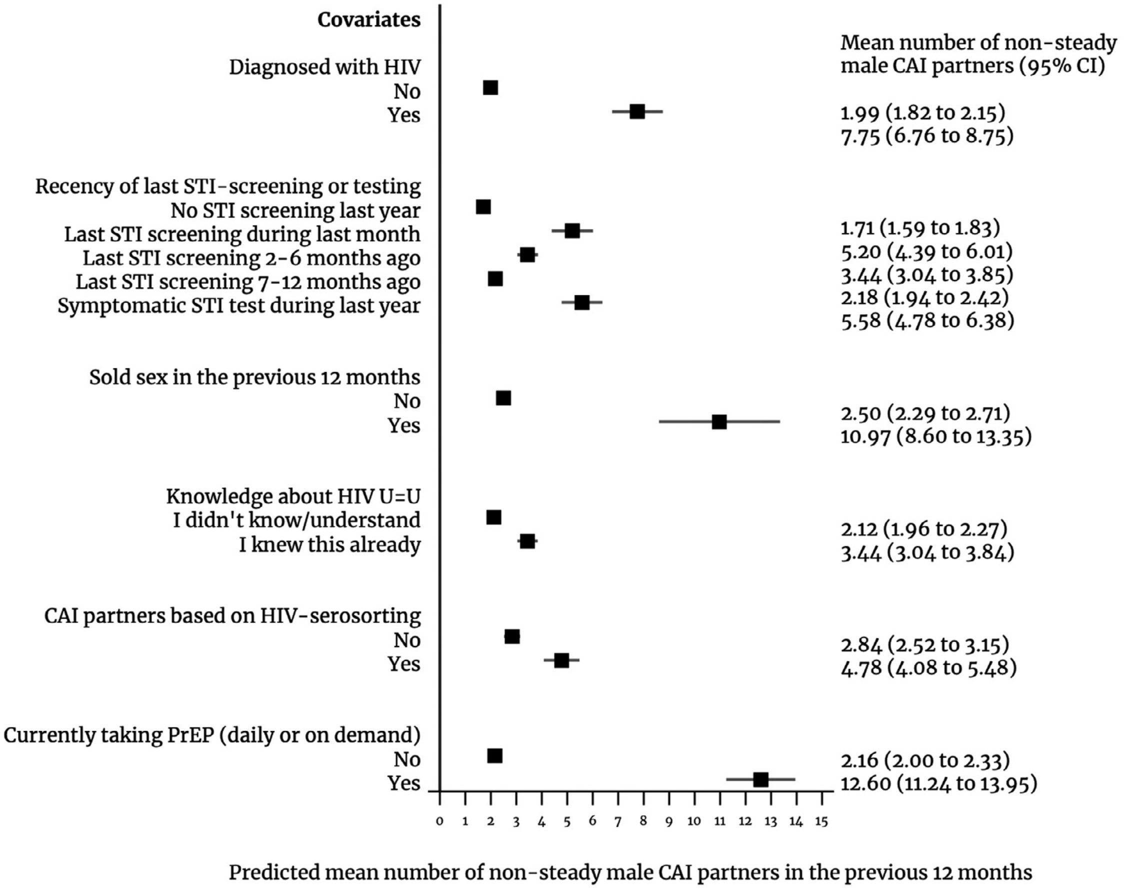

Figure 4. Predicted number of non-steady male CAI partners in the previous 12 months for selected covariates (marginal predicted mean number) in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.

CAI, condomless anal intercourse). Results for covariate measuring PrEP use are only for the year 2017 and the estimates for this covariate are based on a sample size of only 30 countries as in one country (Latvia) there were no PrEP users.

(95%CI: 1.94–2.42), respectively (Figure 4). Those who had a test with symptoms had an incidence rate 3.26 (95%CI: 3.14–3.39) times that of those with no screening in the previous 12 months and a predicted mean number of non-steady male CAI partners of 5.58 (95%CI: 4.78–6.38) (Table 4 and Figure 4).

Engagement in transactional sex was also linked with a higher number of non-steady male CAI partners, particularly among those selling sex (aIRR 4.39, 95%CI: 4.19–4.59), for whom the predicted mean number of partners was 10.97 (95%CI: 8.60–13.35) vs 2.50 (95%CI: 2.29–2.71) partners for those not selling sex. For people selling sex, the number of non-steady male CAI partners rose between waves for all partner number categories above 10 partners or more, almost doubling for more than 50 partners (Table 3). Those buying sex had an incidence rate 1.50 (95%CI: 0.63–1.29) times higher than that of those not paying for sex.

Individuals aware that an HIV undetectable viral load makes the virus untransmissible (U=U), had a higher expected count of non-steady male CAI partners (aIRR 1.63, 95%CI: 1.59–1.66) than those not aware of it (Table 4), whereby the mean predicted number of non-steady male CAI partners for those with knowledge about U=U was 3.44 (95%CI: 3.04–3.84) vs 2.12 for those without it (95%CI: 1.96–2.27) (Figure 4). Individuals practicing HIV-serosorting also had a higher expected number of non-steady male CAI partners (aIRR 1.69, 95%CI: 1.63–1.75) (Table 4), with a predicted number of non-steady male CAI partners of 4.78 (95%CI: 4.08–5.48) vs 2.84 (95%CI: 2.52–3.15) among those not serosorting (Table 4 and Figure 4).

PrEP, syphilis, and CAI

In 2017, PrEP use (daily or on demand) was linked to having substantially higher numbers of non-steady male CAI partners: individuals currently using PrEP had an incidence rate for the count of non-steady male CAI partners 7.90 (95%CI: 6.99–8.94) times that of those who were not using PrEP (Table 5), corresponding to a predicted mean number of partners of 12.60 (95%CI: 11.24–13.95) and 2.16 (95%CI: 2.00–2.33), respectively (Figure 4). This effect did not have a substantial reduction after adjusting for the recency of last screening (aIRR 5.82, 95%CI: 5.29–6.41). In 2017, more than a third (38.60%, 95%CI: 36.93–40.29) of people using PrEP screened for STIs within the previous month, compared to only 6.22% (95%CI: 6.07–6.38) of those who did not take PrEP, and 19.38%

		Association of PrEP use with the number of non-steady CAI partners and probability of syphilis diagnosis		
		Adjusting for sociodemographic and behavioural variables[a] (except STI-screening)	**Adjusting for sociodemographic and behavioural variables[a] (including STI-screening)**	**Adjusting for sociodemographic and behavioural variables[a] (including STI-screening and number of non-steady male CAI partners)**
Incidence rate ratio of the number of non-steady male CAI partners in the previous 12 months	Not currently taking PrEP	reference	reference	
	PrEP daily or on demand	7.902*** (6.987 to 8.936) *N = 77,203*	5.821*** (5.289 to 6.407) *N = 74,309*	N/A
Odds ratio of syphilis diagnosis in the previous 12 months [b]	Not currently taking PrEP	reference	reference	reference
	PrEP daily or on demand	3.018*** (2.298 to 3.962) *N = 79,416*	1.610** (1.198 to 2.164) *N = 76,535*	1.199 (0.894 to 1.607) *N = 73,456*

***Table 5*: Association of PrEP use (currently using PrEP daily or on demand vs not currently using PrEP) with the incidence rate ratio of condomless anal intercourse (CAI) non-steady partners within the previous 12 months, and odds ratio of syphilis diagnosis, in 30 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017.**

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$; 95% confidence intervals in brackets; robust standard errors adjusted by country; CAI, condomless anal intercourse.
Note: sample size includes only responses for 2017 and eligible PrEP users (*i.e.*, HIV-diagnosed respondents are excluded from the sample); sample includes only 30 countries as in one country (Latvia) there were no PrEP users.

[a] Models adjusted for all covariates shown in Table 2.

[b] Models adjusted for language of questionnaire.

(95%CI: 18.65–20.12) of people living with diagnosed HIV; almost two thirds of PrEP users had screened for STIs within the previous six months (Table 3).

In 2017, the proportion of respondents using PrEP reporting a syphilis diagnosis (13.81%, 95%CI: 12.67–15.03) was almost five-fold that of respondents not using PrEP (2.84%, 95%CI: 2.74–2.95) (Figure 2 and Table 3). PrEP use was linked to a greater odds of syphilis diagnosis (aOR 3.08, 95%CI: 2.30–3.96), after adjusting for sociodemographic factors, HIV diagnosis, and engagement in transactional sex. To assess the role of STI-screening and number of non-steady male CAI partners as effect mediators of the association between PrEP use and syphilis diagnosis, we controlled for these factors observing that the effect size substantially reduced and that the association did not hold (aOR 1.20, 95%CI: 0.84–1.61).

Robustness checks

We performed a series of robustness checks by fitting alternative models (multivariable linear probability and multivariable linear regression models) and by testing our model specifications by removing cases with discrepant data (Supplemental data: Appendix 2-6). In each case, our results did not substantially change.

Discussion

Our study shows that self-reported syphilis diagnoses have risen markedly among MSM responding to EMIS. The rise was across all European countries, except for Luxembourg, which is likely to be attributable to non-captured sampling effects. Syphilis diagnoses were strongly associated with living with diagnosed HIV, taking PrEP, and selling sex, and the rise in syphilis diagnoses has disproportionately impacted HIV-diagnosed MSM and MSM sex workers (no longitudinal data on PrEP users can be calculated due to the non-availability of PrEP in 2010). Major determinants associated with increased syphilis diagnoses were more recent STI-screening uptake and increased number of non-steady male CAI partners, both higher in 2017 compared to 2010, and both variables mediating the association between PrEP use and higher chance of syphilis diagnosis. MSM who were PrEP users, HIV-diagnosed, or sex workers reported the highest rates of STI-screening uptake and number of non-steady male CAI partners (confirming results of a previous analysis),[16] which may explain the triple concentration of syphilis in these three population subgroups.

Behavioural changes associated with the syphilis epidemics may partly be due to the evolving consensus on the effectiveness of treatment as prevention: undetectable equals untransmissible and PrEP altering the need for condom in HIV serodiscordant sexual relationships. While we found the number of non-steady male CAI partners to be a mediator of the association between PrEP use and higher odds of syphilis diagnosis, this study was not able to discern whether individuals using PrEP were already having higher numbers of non-steady male CAI partners before initiating PrEP. If this was the case, there has been correct population targeting of the intervention, considering that CAI is a major reason these individuals seek, and clinicians recommend, PrEP use. Nor can it show whether use of PrEP led to increases in number of CAI partners. Further research could longitudinally investigate behaviour changes following PrEP use and their link to increases in syphilis incidence. Recent STI-screening was a key factor of syphilis diagnoses. Individuals screened for STIs more recently reported higher numbers of non-steady male CAI partners, indicating more syphilis-screening among MSM with more risky sexual behaviour, such as PrEP users, HIV-diagnosed individuals, and people selling sex, with higher numbers of non-steady male CAI partners. Medical monitoring of people living with HIV and, even more so, in PrEP users include sexual health counselling and routine STI-screening, which can contribute to diagnosing and treating STIs in highly exposed MSM.[26] Many European countries already recommend three-monthly syphilis-screening in PrEP users, *e.g.* the United Kingdom.[29] However, restricting more regular syphilis-screening in MSM to individuals already included in clinical follow-up (such as MSM diagnosed with HIV or PrEP users) might not be enough to control the syphilis epidemic in MSM. Some countries, therefore, explicitly recommend biannual syphilis-screening in multi-partners MSM.[30,31]

Our study has several limitations. The study sample is likely not representative of all MSM. The online recruitment strategy over-samples more sexually active MSM, those who use the internet and/or dating apps to meet sexual partners.[32] Nevertheless, estimates of national HIV prevalence from EMIS-2010 were strongly correlated with existing estimates based on biological measurement and modelling studies using surveillance data.[33]

Second, there are likely other determinants of syphilis acquisition not included in our models, such as sexual locations (*e.g.*, house-parties, saunas) and use of typical chemsex drugs,[17,18] or that were not measured in both EMIS surveys (*e.g.*, group sex, combining sex and drugs; and anti-LGBT structural stigma).[34]

Third, potential response biases could understate or overstate individual risk on several dimensions, including the total number of male sexual and CAI partners, and/or paying for or selling sex. Measurement bias can also arise in self-reports where respondents omit or incorrectly report the time of syphilis diagnosis. Stigma, social desirability and recall bias may all play a part. The anonymous online format of the survey may have minimized some of these biases. Measurement error makes it harder to detect statistical relationships should they actually exist, as a result biasing our estimated effect sizes in a conservative direction.

Fourth, there was a non-trivial proportion of cases with discrepant data, which involved anomalous or inconsistent reporting of age and partner numbers. However, their inclusion or exclusion did not alter the study's main findings.

Fifth, data on syphilis diagnosis does not include information on type of diagnostic assay. However, between survey waves, there were no major advances in syphilis diagnostic tests, so that any potential bias is likely to be non-differential with regard to our research question.

Clinical implications derived from our results are that MSM disclosing multiple CAI partners should be offered syphilis-screening due to their clearly increased risk and the serious possible sequelae of syphilis. Guidelines for people using PrEP include frequent syphilis-screening, for which our finding that over a third of PrEP users screened within the previous month provides support for the feasibility of implementing a regular HIV- and syphilis-screening approach. Further, community-based education in MSM communities is needed to increase knowledge of and social norms for syphilis-screening. Approaches to foster syphilis-screening, such as online tools for risk assessment, home-sampling, and free at-point-of use tests for men without a previous history of syphilis, along with tools for partner notification to interrupt transmission chains, could be considered as additional combined interventions for national syphilis control and elimination strategies.

Contributors

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Data sharing statement

The EMIS-2017 dataset used for this analysis has been obtained from the London School of Hygiene and Tropical Medicine under a data transfer agreement that prohibits to sharing the dataset publicly. Although we cannot make study data publicly accessible at the time of publication, all authors commit to make the data underlying the findings of the study available in compliance with the Lancet Data Availability Policy. Data requests should be addressed to the London School of Hygiene and Tropical Medicine Research Operations Office Data Management Lead: alex.hollander@lshtm.ac.uk, the last author (axel.schmidt@lshtm.ac.uk), and the Principal Investigator of EMIS-2017 (Peter.Weatherburn@lshtm.ac.uk). Individuals requesting data should present their research objective(s) and enclose a list of requested variables. To protect the confidentiality of participants, data sharing is contingent upon appropriate data handling and good scientific practice by the person requesting the data and should furthermore be in accordance with all applicable local requirements. The London School of Hygiene and Tropical Medicine administrative offices are located at Keppel Street, London WC1E 7HT, United Kingdom.

Declaration of interests

We declare no competing interests.

Ethics committee approval

This study used secondary data and needed no ethical approval.

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Supplementary materials

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References

1 European Centre for Disease Prevention and Control. *Syphilis: ECDC Annual Epidemiological Report for 2018*. Stockholm: European Centre for Disease Prevention and Control; 2020.

2 Savage E. Syphilis and gonorrhoea in men who have sex with men: a European overview. *Euro Surveill*. 2009;14:19417.

3 Abara WE, Hess KL, Fanfair RN, Bernstein KT, Paz-Bailey G. Syphilis trends among men who have sex with men in the United States and Western Europe: a systematic review of trend studies published between 2004 and 2015. *PLoS One*. 2016;11(7):e0159309. https://doi.org/10.1371/journal.pone.0159309.

4 Robert Koch Institut. *SurvStat 2.0*. Robert Koch Institut; 2022.

5 Jebbari H, Simms I, Conti S, et al. Variations in the epidemiology of primary, secondary and early latent syphilis, England and Wales: 1999 to 2008. *Sex Transm Infect*. 2011;87(3):191–198.

6 Health Protection Scotland. Syphilis in Scotland. *Update, 2020*. Edinburgh: Health Protection Scotland, NHS National Services Scotland; 2019.

7 Ndeikoundam Ngangro N, Viriot D, Fournet N, et al. Bacterial sexually transmitted infections in France: recent trends and patients' characteristics in 2016. *Euro Surveill*. 2019;24(5):pii=1800038. https://doi.org/10.2807/1560-7917.ES.2019.24.5.1800038.

8 Caugant D, Kløvstad H, Nilsen Ä, Whittaker R. *Årsrapport 2019 Overvåkning av Seksuelt Overførbare Infeksjoner [2019 Annual Surveillance Report for Sexual Transmitted Infections]*. Oslo: Folkehelseinstituttet; 2020.

9 Tsuboi M, Evans J, Davies EP, et al. Prevalence of syphilis among men who have sex with men: a global systematic review and meta-analysis from 2000–20. *Lancet Glob Health*. 2021;9(8):e1110–e1118.

10 Malek R, Mitchell H, Furegato M, et al. Contribution of transmission in HIV-positive men who have sex with men to evolving epidemics of sexually transmitted infections in England: an analysis using multiple data sources, 2009-2013. *Eurosurveillance*. 2015;20(15):7–15.

11 Dougan S, Evans BG, Elford J. Sexually transmitted infections in Western Europe among HIV-positive men who have sex with men. *Sex Transm Dis*. 2007;34(10):783–790.

12 Fenton KA, Imrie J. Increasing rates of sexually transmitted diseases in homosexual men in Western europe and the United States: why? *Infect Dis Clin North Am*. 2005;19(2):311–331.

13 Jansen K, Schmidt AJ, Drewes J, Bremer V, Marcus U. Increased incidence of syphilis in men who have sex with men and risk management strategies, Germany, 2015. *Euro Surveill*. 2016;21(43):30382.

14 Marcus U, Bremer V, Hamouda O, et al. Understanding recent increases in the incidence of sexually transmitted infections in men having sex with men: changes in risk behavior from risk avoidance to risk reduction. *Sex Transm Dis*. 2006;33(1):11–17.

15 Van de Laar M, Spiteri G. Increasing trends of gonorrhoea and syphilis and the threat of drug-resistant gonorrhoea in Europe. *Eurosurveillance*. 2012;17(29):20225.

16 Marcus U, Mirandola M, Schink SB, Gios L, Schmidt AJ. Changes in the prevalence of self-reported sexually transmitted bacterial infections from 2010 and 2017 in two large European samples of men having sex with men-is it time to re-evaluate STI-screening as a control strategy? *PLoS One*. 2021;16(3):e0248582.

17 Schmidt AJ, Bourne A, Weatherburn P, Reid D, Marcus U, Hickson F. Illicit drug use among gay and bisexual men in 44 cities: Findings from the European MSM Internet Survey (EMIS). *Int J Drug Policy*. 2016;38:4–12.

18 Berg RC, Weatherburn P, Marcus U, Schmidt AJ. Links between transactional sex and HIV/STI-risk and substance use among a large sample of European men who have sex with men. *BMC Infect Dis*. 2019;19(1):686.

19 Golden MR, Dombrowski JC. Syphilis control in the postelimination era: implications of a new syphilis control initiative for sexually transmitted disease/human immunodeficiency virus programs. *Sex Transm Dis*. 2018;45:S86–S92.

20 Nicoll A, Hamers FF. Are trends in HIV, gonorrhoea, and syphilis worsening in western Europe? *BMJ*. 2002;324(7349):1324–1327.

21 European Centre for Disease Prevention and Control. *Surveillance Atlas of Infectious Diseases*. Stockholm: European Centre for Disease Prevention and Control; 2022.

22 The EMIS Network. *EMIS 2010: The European Men-Who-Have-Sex-With-Men Internet Survey. Findings from 38 countries*. Stockholm: European Centre for Disease Prevention and Control; 2013.

23 The EMIS Network. *EMIS-2017 — The European Men-Who-Have-Sex-With-Men Internet Survey. Key Findings from 50 Countries*. Stockholm: European Centre for Disease Prevention and Control; 2019.

24 Weatherburn P, Schmidt AJ, Hickson F, et al. The European men-who-have-sex-with-men internet survey (EMIS): design and methods. *Sexual Res Soc Policy*. 2013;10(4):243–257.

25 Weatherburn P, Hickson F, Reid DS, Marcus U, Schmidt AJ. European men-who-have-sex-with-men internet survey (EMIS-2017): design and methods. *Sexual Res Soc Policy*. 2019:243–257. https://doi.org/10.1007/s13178-013-0119-4.

26 Doran J, Weatherburn P, Hickson F, Marcus U, Reid D, Schmidt AJ. An update on the performance of STI services for gay and bisexual men across European cities: results from the 2017 European MSM Internet Survey. *Sex Transm Infect*. 2021;97(3):201–208.

27 Mendez-Lopez A, Hickson F, Jansen K, et al. What is the empirical basis for converting banded ordinal data on numbers of sex partners among MSM into a continuous scale level variable? A secondary analysis of 13 surveys across 17 countries. *BMC Med Res Methodol*. 2022;22(1):59.

28 StataCorp. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LP; 2019.

29 Brady M, Rodger A, Asboe D, et al. BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2018. *HIV Med*. 2019;20(S2):S2–S80.

30 Schmidt AJ, Rasi M, Esson C, et al. The Swiss STAR trial - an evaluation of target groups for sexually transmitted infection screening in the sub-sample of men. *Swiss Med Wkly*. 2020;150:w20392.

31 Balakrishna S, Salazar-Vizcaya L, Schmidt AJ, et al. Assessing the drivers of syphilis among men who have sex with men in Switzerland reveals a key impact of screening frequency: a modelling study. *PLoS Comput Biol*. 2021;17(10):e1009529.

32 Prah P, Hickson F, Bonell C, et al. Men who have sex with men in Great Britain: comparing methods and estimates from probability and convenience sample surveys. *Sex Transm Infect*. 2016;92(6):455.

33 Marcus U, Hickson F, Weatherburn P, Schmidt AJ. Prevalence of HIV among MSM in Europe: comparison of self-reported diagnoses from a large scale internet survey and existing national estimates. *BMC Public Health*. 2012;12:978.

34 Pachankis JE, Hatzenbuehler ML, Berg RC, et al. Anti-LGBT and anti-immigrant structural stigma: an intersectional analysis of sexual minority men's HIV risk when migrating to or within Europe. *J Acquir Immune Defic Syndr*. 2017;76(4):356–366.

2.2 Study 2: What is the empirical basis for converting banded ordinal data on numbers of sex partners among MSM into a continuous scale level variable? A secondary analysis of 13 surveys across 17 countries

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RESEARCH

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What is the empirical basis for converting banded ordinal data on numbers of sex partners among MSM into a continuous scale level variable? A secondary analysis of 13 surveys across 17 countries

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Abstract

Background: To provide empirically based guidance for substituting partner number categories in large MSM surveys with mean numbers of sexual and condomless anal intercourse (CAI) partners in a secondary analysis of survey data.

Methods: We collated data on numbers of sexual and CAI partners reported in a continuous scale (write-in number) in thirteen MSM surveys on sexual health and behaviour across 17 countries. Pooled descriptive statistics for the number of sexual and CAI partners during the last twelve ($N = 55{,}180$) and 6 months ($N = 31{,}759$) were calculated for two sets of categories commonly used in reporting numbers of sexual partners in sexual behaviour surveys.

Results: The pooled mean number of partners in the previous 12 months for the total sample was 15.8 partners (SD = 36.6), while the median number of partners was 5 (IQR = 2–15). Means for number of partners in the previous 12 months for the first set of categories were: 16.4 for 11–20 partners (SD = 3.3); 27.8 for 21–30 (SD = 2.8); 38.6 for 31–40 (SD = 2.4); 49.6 for 41–50 (SD = 1.5); and 128.2 for 'more than 50' (SD = 98.1). Alternative upper cut-offs: 43.4 for 'more than 10' (SD = 57.7); 65.3 for 'more than 20' (SD = 70.3). Self-reported partner numbers for both time frames consistently exceeded 200 or 300. While there was substantial variation of overall means across surveys, the means for all chosen categories were very similar. Partner numbers above nine mainly clustered at multiples of tens, regardless of the selected time frame. The overall means for CAI partners were lower than those for sexual partners; however, such difference was completely absent from all categories beyond ten sexual and CAI partners.

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Conclusions: Clustering of reported partner numbers confirm common MSM sexual behaviour surveys' questionnaire piloting feedback indicating that responses to numbers of sexual partners beyond 10 are best guesses rather than precise counts, but large partner numbers above typical upper cut-offs are common.

Keywords: Sexual behaviour, Men-who-have-sex-with-men, Survey research

Background

Survey designers and statisticians often have distinct needs when it comes to the choice of ordinal or continuous scale level variables for measuring sexual behaviours, for example, numbers of sexual or condomless anal intercourse (CAI) partners.

In sexual behaviour surveys with men who have sex with men (MSM), piloting survey questions on partner numbers has shown that men struggle with reporting precise partner numbers when they had ten or more partners in the past six or twelve months [1, 2]. Instead, respondents provide rounded estimates rather than precise counts when reporting numbers of partners beyond nine. For this reason, many surveys today use a mixture of continuous and ordinal scales, starting with a continuous scale format for partner numbers between 0 and 9 (or 10, or 19, or 20), and switching to categories thereafter.

For example, the European MSM Internet Survey (EMIS), the largest survey on sexual behaviour and sexual health among MSM worldwide, used the following answer format: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11–20, 21–30, 31–40, 41–50, more than 50 for reporting sexual partner numbers [1]. However, statisticians often prefer calculating the attributable risk for each additional partner, for which a continuous scale variable is needed. The last category, be it 'more than 10', 'more than 20', or 'more than 50' is particularly difficult as the average number beyond this cut-off is unknown.

The aim of this study is to explore the clustering of reported numbers of sexual partners in studies with an open answer format, and to provide an empirical basis for substituting categories of partner numbers with their probable mean. This exercise allows us to explore the validity of alternative designs of survey questions and potential sources of bias in questionnaire design and respondents' reporting in sexual behaviour surveys, providing methodological insights in sexual behaviour research.

Methods

Data sources

We collated data on number of sexual partners reported in a continuous scale in MSM surveys on sexual health and behaviour. We contacted epidemiologists and social researchers from the EMIS network [1–3] across Europe and Canada (typically at least one academic and/or governmental partner per country) to identify behavioural surveys among MSM conducted in their respective countries, and asked them which of the national surveys had used open write-in fields for the numbers of sexual partners. Thirteen national and multi-national surveys were identified as eligible, and data of the partner number write-in fields were obtained from these surveys and included in our analyses [4–15]. The surveys were undertaken between 1995 and 2019 across Europe and in Canada.

All surveys asked about the overall number of sexual partners, with four also asking specifically about the number of CAI partners. Eight surveys provided data for numbers of sexual partners over the previous 12 months and five for over the previous 6 months. Table 1 (header) lists all the surveys included, years and countries in which they were performed, type of data collected, and time frame (recall period).

Statistical analyses

Pooled descriptive statistics for the number of sexual partners over the previous 12 months were calculated, first, for the total number of survey respondents and, second, for two sets of commonly used categories for reporting number of sexual partners in sexual behaviour surveys. The first commonly used set of categories included the following bands: 11–20; 21–30; 31–40; 41–50; more than 50 partners (and more than 10; more than 20 as alternative upper cut-offs). The second set included 10–19; 20–29; 30–39; 40–49; 50 or more partners (and 10 or more; 20 or more as alternative upper cut-offs). These are two separate sets of categories with different cut-offs in their bands, thus providing different ranges (e.g., in the first set there is the category 10–19 sexual partners and in the second set there is the category 11–20 sexual partners).

Next, we calculated the mean number of sexual partners by time frame (over the previous 12 months vs. the previous 6 months), by survey (for each of the thirteen included surveys), and by type of sexual partner (any sexual partner vs. CAI partners) for one of the commonly reported set of categories to assess potential differences in the means by each of these aspects and to contrast the robustness of the first findings.

Respondents reporting 'zero' partners were excluded from the overall N and, thus, from the overall mean and all sample share proportions. Respondents with missing data on partner numbers were also excluded.

Table 1 Pooled descriptive statistics for one set of bands for number of sexual partners: detailed estimates by survey, time frame and type of sexual partner

	OVERALL	**HIVHOM-1995–2006**	**GMA-2007**	**SEXHOM-2008**	**EPGL-2011**	**SexNow-2014/15**	**SMMASH-2016**	**London-GMSHS-2019**	**ERAS-2019**	**SMMASH-2016**	**London-GMSHS-2019**	**OVERALL**	**SIALON-2011**	**iCruise-2016**	**MSMSS-2018**	**SexNow-2019**	**ERAS-2019**	**SIALON-2011**	**MSMSS-2018**
Countries	**AT, CA, DE, FR, ES, IE, UK**	**ES**	**AT, DE**	**ES**	**FR**	**CA**	**IE, UK-NIR, UK-SCT, UK-WLS**	**UK-ENG**	**FR**	**IE, UK-NIR, UK-SCT, UK-WLS**	**UK-ENG**	**BE, BG, CA, DE, FR, ES, IT, LT, PL, PT, RO, SE, SK, SI, UK**	**BE, BG, DE, ES, IT, LT, PL, PT, RO, SE, SK, SI, UK**	**CA**	**DE**	**CA**	**FR**	**BE, BG, DE, ES, IT, LT, PL, PT, RO, SE, SK, SI, UK**	**DE**
Partner number categories	**Sexual partners in the previous 12 months**									**CAI partners in the previous 12 months**		**Sexual partners in the previous 6 months**						**CAI partners in the previous 6 months**	
Survey N	55,180	4,220	8,497	1,108	9,648	7,292	3,299	1,231	19,885	1,889	827	31,759	3,676	411	1,926	6,659	19,087	1,392	1,388
Overall Mean	**15.8**	33.7	12.8	23.0	18.8	12.2	13.9	14.4	13.1	5.3	8.2	**8.5**	10.2	11.3	10.2	10.4	7.1	4.8	7.3
N (11–20)	7,460	776	989	220	1,214	1,109	526	153	2,473	87	50	3,095	436	68	256	862	1,473	61	107
Mean (11–20)	**16.4**	16.7	16.5	16.6	16.9	15.9	16.2	17.2	16.2	15.8	17.2	**16.2**	16.8	14.6	16.5	16.0	16.1	16.5	16.6
N (21–30)	3,296	473	413	90	602	427	202	74	1,015	27	20	1,225	149	23	107	340	606	30	37
Mean (21–30)	**27.8**	27.8	27.9	27.3	28.1	27.2	27.5	27.9	27.9	27.4	28.4	**27.4**	27.8	26.0	28.7	27.5	27.1	27.0	28.6
N (31–40)	1,162	195	149	36	176	129	97	19	361	16	13	340	36	14	30	118	142	6	16
Mean (31–40)	**38.6**	38.8	38.4	38.5	38.8	37.9	38.2	38.4	38.8	37.3	38.3	**38.2**	38.9	35.6	39.0	38.1	38.2	37.2	38.9
N (41–50)	1,821	336	206	63	375	148	88	47	558	14	14	496	67	8	30	132	259	4	11
Mean (41–50)	**49.6**	49.5	49.7	49.7	49.7	49.1	49.3	49.9	49.6	47.9	49.7	**49.3**	49.8	46.6	49.8	48.7	49.5	48.8	50.0
N (>50)	2,912	653	338	83	625	208	107	57	841	20	17	536	90	11	48	130	257	11	23
Sample Share	*5.3%*	*15.5%*	*4.0%*	*7.5%*	*6.5%*	*2.9%*	*3.2%*	*4.6%*	*4.2%*	*1.1%*	*2.1%*	*1.7%*	*2.4%*	*2.7%*	*2.5%*	*2.0%*	*1.3%*	*0.8%*	*1.7%*
Mean (>50)	**128.2**	127.9	122.4	147.3	150.1	121.0	126.8	112.3	115.6	122.4	119.7	**107.3**	99.4	104.7	116.8	105.9	109.1	100.3	115.8
Alternative upper cut-offs:																			
N (>10)	16,651	2,433	2,095	492	2,992	2,021	1,020	350	5,248	164	114	5,692	778	124	471	1,582	2,737	112	194
Sample Share	*30.2%*	*57.7%*	*24.7%*	*44.4%*	*31.0%*	*27.7%*	*30.9%*	*28.4%*	*26.4%*	*8.7%*	*13.8%*	*17.9%*	*21.2%*	*30.2%*	*24.5%*	*23.8%*	*14.3%*	*8.0%*	*14.0%*
Mean (>10)	**43.4**	55.0	40.6	46.5	52.4	33.0	35.0	40.5	39.5	35.5	40.9	**31.4**	32.3	29.1	33.0	30.2	31.6	29.8	34.4
N (>20)	9,191	1,657	1,106	272	1,778	912	494	197	2'775	77	64	2,597	342	56	215	720	1,264	51	87
Sample Share	*16.7%*	*39.3%*	*13.0%*	*24.5%*	*18.4%*	*12.5%*	*15.0%*	*16.0%*	*14.0%*	*4.1%*	*7.7%*	*8.2%*	*9.3%*	*13.6%*	*11.2%*	*10.8%*	*6.6%*	*3.7%*	*6.3%*
Mean (>20)	**65.3**	73.0	62.2	70.6	76.6	53.7	55.0	58.6	60.3	57.8	59.3	**49.5**	52.1	46.8	52.7	47.3	49.6	45.7	56.3

Note: Respondents with missing data or reporting 'zero' partners were excluded from the overall N and thus from the overall mean and all sample share proportions. *EPGL* Enquête Presse Gays et Lesbiennes, *ERAS* Enquête Rapport au sexe, *CAI* condomless anal intercourse, *GMA* gay men and AIDS, *GMSHS* gay men sexual health survey, *HIVHOM* Conductas de riesgo en hombres que tienen relaciones sexuales con hombres reclutados por Internet, *MSMSS* MSM Screening Study, *SEXHOM* Monitorizacion bio-conductual en HSH (Catalunya), *SMMASH* Social Media, *MSM* Sexual and Holistic Health study

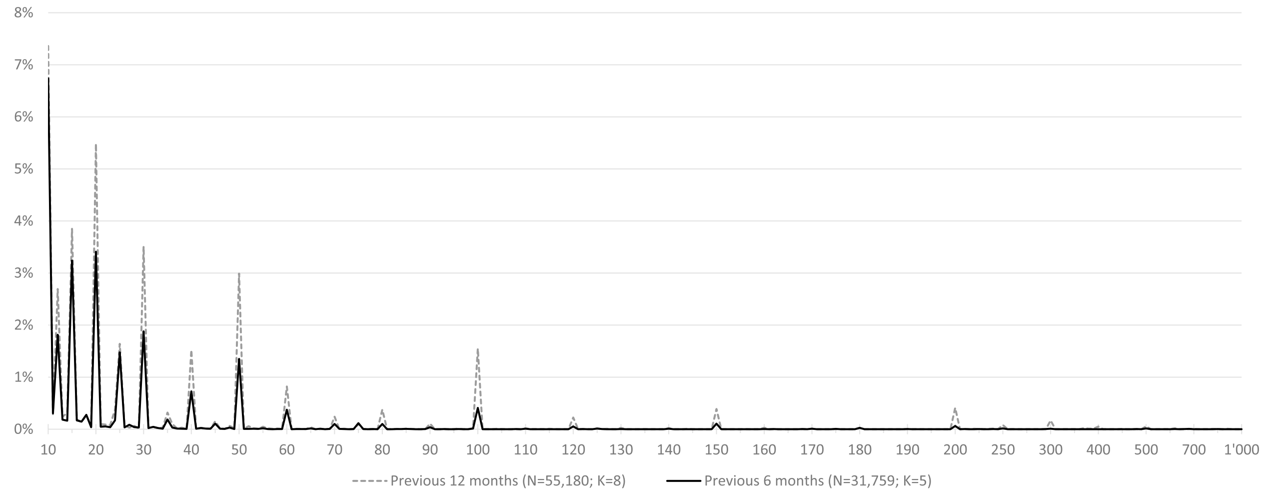

Fig. 1 Distribution of overall male sexual partners among MSM (continuous scale variable). Data shown beyond nine partners only (N, number of respondents; K, number of surveys)

The write-in answer '999' ($N = 29$), which may have represented the researcher code 'missing', and the answers '1000' and '2000' ($N = 11$), which were extreme outliers, were excluded.

Results

Across all surveys, the combined sample size of respondents reporting the number of sexual partners in the previous 12 and previous 6 months was 55,180 and 31,759, respectively.

Figure 1 depicts the distribution of overall male sexual partners among MSM reporting more than nine partners. Across all surveys, the number of partners had an asymmetrical distribution skewed to the right. Self-reported partner numbers for both time frames consistently exceeded 200 or 300. Partner numbers beyond nine mainly clustered at 10, 12, 15, 20, 25, 30, 40, 50, 60, 80, 100, 120, 150, 200, and 300, regardless of the selected time frame.

Table 2 shows the total number and proportion of respondents reporting partners in each category, and pooled descriptive statistics (mean, standard deviation, median, and interquartile range) for each of the two alternative sets of bands. The pooled mean number of partners in the previous 12 months for the total sample was 15.8 partners (SD = 36.6), while the median number of partners was 5 (IQR = 2–15). Means for number of partners in the previous 12 months for the first set of categories were: **16.4** for 11–20 partners (SD = 3.3); **27.8** for 21–30 (SD = 2.8); **38.6** for 31–40 (SD = 2.4); **49.6** for 41–50 (SD = 1.5); and **128.2** for 'more than 50' (SD = 98.1). For the alternative upper cut-offs, mean partner numbers were **43.4** for 'more than 10' (SD = 57.7), and **65.3** for 'more than 20' (SD = 70.3).

Means for the second set of commonly reported categories were: **12.1** for 10–19 partners (SD = 2.4); **21.4** for 20–29 (SD = 2.3); **30.7** for 30–39 (SD = 1.8); **40.9** for 40–49 (SD = 2.2); and **99.9** for '50 or more' (SD = 86.9). For the alternative upper cut-offs, mean partner numbers were **36.8** for '10 or more' (SD = 53.4); **54.1** for '20 or more' (SD = 64.1).

Mean number of sexual partners for the first set of categories (those whose bands commenced with a multiple of ten, e.g. 30–39) consistently resulted in a lower mean compared to the alternative band (those containing a multiple of ten in the upper end of the range, e.g. 31–40). According to the right skewed distribution (Fig. 1), all reported medians are consistently lower than the reported means (Table 2).

Table 1 shows, for each survey considered, the numbers and proportions of respondents reporting partners in each category, and the mean number of partners reported within each category, for both the previous 12 months and previous 6 months, and for both number of sexual partners and number of CAI partners. These data are provided only for one of the commonly used set of categories.

While there was substantial variation across all surveys with respect to the overall mean numbers, the means for all categories were very similar.

Across the two time frames, the overall mean number of sexual partners in the previous 6 months was 54% of the overall mean partner number in the previous 12 months. When moving towards higher partner number categories, this proportion increased steadily to 72% ('more than 10'), 76% ('more than 20'), and 84% ('more than 50').

Irrespective of the time frame, in all surveys providing estimates for the number of sexual and CAI partners, the overall means for CAI partners were lower than those for

Table 2 Pooled descriptive statistics for two sets of alternative bands for number of sexual partner categories: overall estimates for number of sexual partners for all the included MSM surveys

Categories for numbers of sexual partners: EMIS categories		**Categories for numbers of sexual partners: alternative categories**	
Total		**Total**	
N (%)	55,180 (100%)	N (%)	55,180 (100%)
Mean (SD)	15.8 (36.6)	Mean (SD)	15.8 (36.6)
Median (IQR)	5 (2–15)	Median	5 (2–15)
11–20 partners		**10–19 partners**	
N (%)	7460 (13.5%)	N (%)	8497 (15.4%)
Mean (SD)	16.4 (3.3)	Mean (SD)	12.1 (2.4)
Median (IQR)	15 (14–20)	Median	12 (10–15)
21–30 partners		**20–29 partners**	
N (%)	3296 (6.0%)	N (%)	4385 (8.0%)
Mean (SD)	27.8 (2.8)	Mean (SD)	21.5 (2.3)
Median (IQR)	30 (25–30)	Median	20 (20–24)
31–40 partners		**30–39 partners**	
N (%)	1162 (2.1%)	N (%)	2259 (4.1%)
Mean (SD)	38.6 (2.4)	Mean (SD)	30.7 (1.8)
Median (IQR)	40 (37–40)	Median	30 (30–30)
41–50 partners		**40–49 partners**	
N (%)	1821 (3.3%)	N (%)	1011 (1.8%)
Mean (SD)	49.6 (1.5)	Mean (SD)	40.9 (2.2)
Median (IQR)	50 (50–50)	Median (IQR)	40 (40–40)
> 50 partners		**≥ 50 partners**	
N (%)	2912 (5.3%)	N (%)	4561 (8.3%)
Mean (SD)	128.2 (98.1)	Mean (SD)	99.9 (86.9)
Median (IQR)	100 (75–150)	Median (IQR)	70 (50–100)
Alternative upper cut-offs			
> 20 partners		**≥ 20 partners**	
N (%)	9191 (16.7%)	N (%)	12,216 (22.1%)
Mean (SD)	65.3 (70.3)	Mean (SD)	54.1 (64.1)
Median (IQR)	48 (30–70)	Median (IQR)	30 (21–50)
> 10 partners		**≥ 10 partners**	
N (%)	16,651 (30.2%)	N (%)	20,713 (37.5%)
Mean (SD)	43.4 (57.7)	Mean (SD)	36.8 (53.4)
Median (IQR)	25 (16–50)	Median (IQR)	20 (12–40)

Notes: *SD* Standard Deviation, *IQR* Inter-quartile Range

sexual partners. Such difference was absent from all categories beyond ten sexual and CAI partners.

Discussion

Using data from thirteen national and multi-national sexual behaviour surveys among MSM, we looked at the distribution of partner numbers in the previous 12 and 6 months and calculated means for two commonly used sets of partner number categories.

The means and medians for the two sets of commonly reported categories show very different results because of clustering of responses in the tens, which pulled down, or up, the mean and medians toward the tens, whether it was included in the upper or lower limit of the band range. Clustering of reported partner numbers confirm MSM sexual behaviour surveys' questionnaire piloting feedback, such as that from the EMIS [1, 2], that partner numbers beyond nine—and irrespective of the chosen time frame—were best guesses rather than precise counts, with 'twelve', '60', and '120' possibly reflecting 'about one per month', 'about five per month', and 'about ten per month', respectively, in a 12 months retrospective period.

The decreasing difference between means of partner numbers in higher categories across the two time frames may be due to the so-called telescoping effect, a cognitive effect in survey research, whereby there is a temporal displacement of events [16]. In this case events may be perceived as having happened some time nearer or further from the time of interview. This consistently occurred across all included surveys, and this effect may have slightly inflated the reported number of partners in the higher categories of surveys querying about the previous 6 months.

Above nine partners, the mean numbers of sexual and CAI partners were rather similar, suggesting that non-condom use is intermittent during anal sex with a smaller number of partners, but may become more common when dealing with larger numbers of sexual (intercourse) partners.

We found that for the higher categories in both sets of bands, i.e. 'more than 50' / '50 or more', the associated interquartile ranges were wide and the standard deviations were high in relation to the means (Table 2). Given the large dispersion of the distribution in the highest categories of both sets of bands, adding an additional category in the upper range of the sets (for example, a category measuring 51–100 / 50–99 sexual partners and an additional capturing 'more than 100' / '100 or more' sexual partners), may provide greater precision in measurement in surveys collecting data with categorical variables. Greater accuracy in the estimation of the number of sexual partners in the MSM population may contribute to overcoming difficulties in the prevention and control of the HIV/STI epidemics and their risk assessment.

One limitation of this analysis is that our findings may not transfer to MSM behaviour in other countries outside the regions of the countries from the surveys, especially those countries where homosexuality is highly stigmatised. Another limitation is that our selection of MSM surveys was not strictly systematic, however, given the composition of the research network, we consider it unlikely that we missed large European or Canadian surveys that no-one in the network was aware of. Additionally, the time lapse between the earliest and latest surveys is of almost 25 years, a time period throughout which MSM sexual behaviour may have changed due to, for instance, developments in HIV/STI interventions or cultural changes related to reduced stigmatization. Nonetheless, we do not expect the potential omission of a survey or the time lapse between the included surveys to have substantially impacted on the overall results. The large number of surveys included makes our study a comprehensive review and summary of the sexual behaviour in terms of number of sexual partners of MSM in Canada and Europe.

Conclusions

The variations of the calculated means across surveys conducted in different countries, study populations and years were low. Therefore, we believe that the results can serve to foster methodologically robust substitution of partner number categories with probable mean numbers of sexual and CAI partners in MSM-oriented surveys.

Abbreviations

CAI: Condomless anal intercourse; EMIS: European MSM Internet Survey; MSM: Men-who-have-sex-with-men.

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Authors' contributions

AJS and UM conceptualised the analysis, AJS reached out to partners, compiled the data, calculated the numbers, and drafted the manuscript. AML reviewed the statistics, finalised the manuscript and the tables, and wrote the abstract. All authors reviewed and contributed to the manuscript. AJS, FH, PW, UM et al. conducted EMIS-2010 and 2017; AJS, UR et al. conducted GMA-2007; KJ et al. conducted MSMSS-2018; NL et al. conducted SexNow-2014/15/19; FB et al. conducted London-GMSHS-2019; CF et al. conducted HIVHOM-1995–2006 and SEXHOM-2008; AV et al. conducted EPGL-2011 and ERAS-2019; MM, LG, CF, UM et al. conducted SIALON-2011; JF et al. conducted SMMASH-2016, DJB et al. conducted iCruise-2016. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Weatherburn P, Hickson F, Reid DS, Marcus U, Schmidt AJ. European men-who-have-sex-with-men internet survey (EMIS-2017): design and methods. Sex Res Soc Policy. 2020;17:543–57. https://doi.org/10.1007/s13178-019-00413-0.
2. Weatherburn P, Schmidt AJ, Hickson F, Reid D, Berg RC, Hospers HJ, et al. The European men-who-have-sex-with-men internet survey (EMIS): design and methods. Sex Res Soc Policy. 2013;10(4):243–57.

3. EMIS network. European Men-who-have-sex-with-men Internet Suvey 2017 website. 2017 [Available from: www.emis2017.eu].
4. Folch C, Muñoz R, Zaragoza K, Casabona J. Sexual risk behaviour and its determinants among men who have sex with men in Catalonia, Spain. Eurosurveillance. 2009;14(47):19415.
5. Méthy N, Velter A, Semaille C, Bajos N. Sexual behaviours of homosexual and bisexual men in France: a generational approach. PLoS One. 2015;10(3):e0123151–e.
6. Gios L, Mirandola M, Toskin I, Marcus U, Dudareva-Vizule S, Sherriff N, et al. Bio-behavioural HIV and STI surveillance among men who have sex with men in Europe: the Sialon II protocols. BMC Public Health. 2016;16(1):212.
7. Frankis J, Flowers P, McDaid L, Bourne A. Low levels of chemsex among men who have sex with men, but high levels of risk among men who engage in chemsex: analysis of a cross-sectional online survey across four countries. Sex Health. 2018;15(2):144–50.
8. Logan L, Fakoya I, Howarth A, Murphy G, Johnson AM, Rodger AJ, et al. Combination prevention and HIV: a cross-sectional community survey of gay and bisexual men in London, October to December 2016. Euro Surveill. 2019;24(25):1800312.
9. Card KG, Fournier AB, Sorge JT, Morgan J, Grace D, Ham D, et al. Substance use patterns and awareness of biomedical HIV prevention strategies among sexual and gender minority men in Canada. AIDS Care. 2020;32(12):1506–14.
10. Jansen K, Steffen G, Potthoff A, Schuppe A-K, Beer D, Jessen H, et al. STI in times of PrEP: high prevalence of chlamydia, gonorrhea, and mycoplasma at different anatomic sites in men who have sex with men in Germany. BMC Infect Dis. 2020;20(1):110.
11. Duchesne L, Lydié N, Velter A. Increase in the overall level of protected anal sex in men who have sex with men in France: results from the repeated cross-sectional survey rapport au Sexe, France, 2017-2019. AIDS Care. 2020;32(sup2):162–9.
12. Brennan DJ, Kesler M, Lachowsky NJ, Davies A, Georgievski G, Adam BD, et al. Sociodemographic and Psychological Predictors of Seeking Health Information Online among GB2M in Ontario: Findings from the #iCruise Project, International Journal of Sexual Health. 2021. https://doi.org/10.1080/19317611.2021.2000087.
13. Bochow M, Schmidt AJ, Grote S. Schwule Männer und HIV/AIDS: Lebensstile, Szene, Sex 2007. Ein Befragung im Auftrag der Bundeszentrale für gesundheitliche Aufklärung, Köln. Belin: AIDS-Forum DAH; 2010.
14. Centre d'Estudis Epidemiològics sobre la Sida de Catalunya (CEESCAT). Informe epidemiològic biennal CEEISCAT. Sistema integrat de vigilància epidemiològica de la SIDA/VIH/ITS a Catalunya. SIVES 2010. Barcelona: Generalitat de Catalunya, Departament de Salut; 2011.
15. Ferlatte O, Salway T, Trussler T, Oliffe JL, Gilbert M. Combining intersectionality and syndemic theory to advance understandings of health inequities among Canadian gay, bisexual and other men who have sex with men. Crit Public Health. 2018;28(5):509–21.
16. Kupek E. Bias and heteroscedastic memory error in self-reported health behavior: an investigation using covariance structure analysis. BMC Med Res Methodol. 2002;2(1):14.

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2.3 Study 3: Prevalence and sociodemographic determinants of public stigma towards people with HIV and its impact on HIV testing uptake: A cross-sectional study in 64 low- and middle-income countries

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ORIGINAL ARTICLE

Prevalence and sociodemographic determinants of public stigma towards people with HIV and its impact on HIV testing uptake: A cross-sectional study in 64 low- and middle-income countries

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Abstract

Background: HIV stigma and discrimination are drivers of adverse HIV outcomes because they deter individuals from engaging in the HIV care continuum. We estimate the prevalence of public stigma towards people with HIV, investigate individuals' sociodemographic determinants for reporting stigmatizing attitudes, and test the impact of HIV stigma on HIV testing uptake.

Methods: This was an observational study based on an analysis of cross-sectional surveys from 64 low- and middle-income countries. We used nationally representative survey data for the population aged 15–49 years from 2015 to 2021, which was the latest available data. HIV public stigma was measured using an index of two questions about attitudes towards people with HIV. First, prevalence estimates of HIV stigma were calculated by country, across countries, and by sociodemographic characteristics. Second, country fixed-effects multivariable logistic regression models were fit to assess sociodemographic determinants of holding stigmatizing attitudes towards people with HIV. Additional logistic regression models assessed country-level income and HIV prevalence as determinants of stigma and assessed the role of HIV public stigma as a driver of testing uptake.

Results: A total of 1 172 841 participants were included in the study. HIV stigma was prevalent in all countries, ranging from 12.87% in Rwanda to 90.58% in Samoa. There was an inverse dose–response association between HIV stigma and educational level, wealth quintile, and age group, whereby higher levels of each were associated with lower odds of holding stigmatized attitudes towards people with HIV. The odds of stigmatized attitudes were lower among men and individuals with adequate knowledge of HIV. HIV stigma was lower in countries with greater gross domestic product per capita and HIV prevalence. Holding stigmatized attitudes towards people with HIV was associated with lower testing uptake, including having ever tested or having tested in the last year.

Conclusion: HIV stigma is present to a highly varying degree in all countries studied, so different approaches to reducing stigma towards people with HIV are required across settings. Action to eliminate HIV stigma is crucial if we are to progress towards ending HIV because holding stigmatized attitudes towards people with HIV was associated with reduced testing.

KEYWORDS

HIV, low- and middle-income countries, social determinants of health, sociodemographic inequities, stigma, testing

INTRODUCTION

HIV stigma and discrimination are recognized as key barriers to addressing the HIV epidemic because they affect the lives, health, and wellbeing of people with HIV and, in turn, of society as a whole [1]. The Joint United Nations Programme on HIV/AIDS (UNAIDS) Global AIDS Strategy 2021–2026 set the goal of ending stigma and discrimination towards people living with and affected by HIV [2, 3]. Similarly, the World Health Organization (WHO) recognizes the importance of international goal setting to reduce stigma. The WHO global health sector strategies on, respectively, HIV, viral hepatitis, and sexually transmitted infections (STIs) 2022–2030 set 2030 country targets that "less than 10%" of people with HIV experience HIV-related stigma. Despite progress in the treatment and prevention of HIV, people with HIV continue to experience negative attitudes, beliefs, and behaviours based on their HIV status, leading to a range of negative social and health outcomes, including decreased access to healthcare, reduced quality of life, and increased vulnerability to HIV transmission. The impact of stigma and discrimination is not limited to individual experiences but also extends to public health and societal outcomes, hindering efforts to end the HIV epidemic [4].

HIV-related stigma refers to negative attitudes and beliefs held by individuals or society towards people with HIV. Stigma can occur in different forms. One form is public stigma, which is the stigma held by members of society towards people with HIV, including in interpersonal relationships [5–7]. Discrimination refers to actions that restrict the rights, opportunities, and access to resources of people with HIV based on these negative attitudes and beliefs.

Stigma and discrimination towards people with HIV impact the HIV response throughout the HIV care continuum. Stigma and discrimination can deter individuals from testing for HIV, which means that people with HIV either do not get tested at all or experience delays in being diagnosed with HIV. This has additional major cascading effects, resulting in people not accessing HIV treatment and ultimately not achieving viral suppression [8–11], the key pillars of the global 95–95–95 HIV targets for ending AIDS [2]. Stigma and discrimination towards people with HIV can also deter individuals from accessing HIV prevention and broader sexual health services [11]. Additionally, stigma and discrimination deteriorate the health-related quality of life of people with HIV [12, 13] and exacerbate multimorbidity, including poor mental health [11, 14, 15]. Social rejection based on HIV serostatus may also drive mental health deterioration through social isolation, low self-esteem, and adverse socioeconomic outcomes, deepening social and health inequalities by HIV status [14, 15].

Knowledge of the occurrence of stigmatized and discriminatory attitudes towards people with HIV and the characteristics of this population can provide insights for targeted interventions to reduce stigma and discrimination towards ending HIV and achieving long-term wellbeing [16]. Here, we measure the societal prevalence of stigmatized and discriminatory attitudes towards people with HIV in 64 countries and assess individuals' sociodemographic determinants for reporting public HIV stigma. Finally, we quantify the impact of this reported public stigma on HIV testing.

MATERIALS AND METHODS

Study design and participants

We conducted an analysis of cross-sectional surveys covering 64 low- and middle-income countries using the latest available data from the period 2015 to 2021 from Demographic and Health Surveys (DHS) [17] from round VII or Multiple Indicator Cluster Surveys (MICS) from round 6. DHS and MICS provide nationally representative survey microdata collected through probabilistic sampling. We included surveys from the latest DHS and MICS rounds as they share common questions on HIV public stigma and provide the most recent data.

We constructed an analysis sample that included all women and men aged between 15 and 49 years at the time of the survey who had data on the main outcome variable (in a few countries, the questionnaire's HIV module was only asked to a nationally representative sub-population). Eleven countries only had data from women, and one country only had data from ever-married men and women. The included countries were those classified as low- or middle-income countries at the time of survey implementation according to the World Bank country classification by income level [18]. Appendix A1 provides details on the sample characteristics and size for each country.

Outcomes

The main outcome variable was stigmatizing and discriminatory attitudes towards people with HIV, also referred to as HIV public stigma or, here onwards, HIV stigma. HIV stigma was measured as an index of two questions about attitudes towards people with HIV. Previous efforts by UNAIDS to monitor HIV stigma and discrimination have used this measurement approach [19].

Response to the main outcome was dependent on the respondent having ever heard of HIV (i.e., individuals who had never heard of HIV were filtered out of the survey module on HIV). The first question asked whether the respondent would buy fresh vegetables from a shopkeeper or vendor who is HIV positive, for which the possible responses were 'yes', 'no', or 'don't know/not sure/it depends'. The second question asked whether the respondent thought that children living with HIV should be allowed to attend school with children who do not have HIV. The possible responses included 'yes', 'no', or 'do not know/not sure/it depends'. There were minor variations in the questions across surveys: in a few countries, the questions referred to 'AIDS' instead of 'HIV' or to 'students' instead of 'children', according to the English, Spanish, Portuguese, or French questionnaire versions.

We defined HIV stigma as clearly stated stigmatizing and discriminatory attitudes towards people with HIV, following the UNAIDS measurement approach [19]. Thus, a response denoting stigmatized or discriminatory attitudes towards people with HIV to any of the two questions (i.e., they would not buy vegetables from a shopkeeper who is HIV positive or thought children living with HIV should not attend school with children who do not have HIV) was classified as holding HIV public stigma. All remaining responses reporting no stigmatized attitudes and/or doubt (i.e., 'don't know/not sure/it depends') were classified as 'no HIV stigma/don't know'. There were missing data when a respondent refused to answer either or both of the two questions on HIV stigma.

Two secondary outcomes measured HIV testing uptake: having ever tested for HIV and having tested for HIV in the past year.

Correlates

We assessed five sociodemographic variables as determinants of holding stigmatized and discriminatory attitudes towards people with HIV. These variables included sex (woman or man), age (15–19, 20–29, 30–39, and 40–49 years), educational level (none or pre-primary, primary, secondary, and higher), wealth quintile (ranging from poorest to highest quintile), and geographical location (urban and rural).

We measured individuals' knowledge about HIV through an index of six variables, following a similar approach used by the DHS and MICS programmes [20]. These variables were included in the index based on the available data in the DHS and MICS databases and were based on questions consistently asked across surveys, allowing for cross-country comparability. The questions were about whether one can avoid HIV by having only one faithful uninfected partner, can get HIV from a mosquito bite, can avoid HIV by using a condom correctly every time, can get HIV by sharing food with a person who has HIV, whether a healthy-looking person may have HIV, and fear of getting HIV in contact with the saliva of an infected person. Individuals who responded correctly to all questions on knowledge of HIV were classified as having comprehensive basic knowledge; an incorrect response to any question classified the respondents as not having a comprehensive basic knowledge of HIV.

Gross domestic product (GDP) per capita and HIV prevalence were measured at the country level using data from the World Bank Development Indicators database for the years 2019 and 2021 [21]. GDP was measured in 2017 international dollars per capita adjusted for purchasing power parity. Data on country population size for the year 2019 were taken from the United Nations Population Division population estimates database [22].

Statistical analysis

Analyses excluded individuals with missing data on HIV public stigma and individuals outside the age range of interest (15–49 years, which is the common age group surveyed in DHS and MICS except for a few countries that included respondents aged >49 years).

Prevalence estimates of HIV public stigma were first calculated by country and then pooled across all 64 countries and by groups based on sociodemographic characteristics. All prevalence estimates were weighted using individual-level weights. Cross-national pooled prevalence estimates (overall and by sociodemographic characteristics) were additionally weighted using country-level weights for the sample data to represent the population of the included countries. This country weight was calculated using the country population as the reciprocal of the likelihood of being sampled. The population for each country matched the sex (women and men or only women) and age groups (15–49 years) of the country sample (Appendix A1). The country total samples included cases with missing data to account for non-response bias in the country-level weight.

Second, fixed-effects multivariable logistic regression models were fit to assess sociodemographic characteristics and HIV knowledge as determinants of public stigma towards people with HIV. Models estimated adjusted odds ratios (aORs) in a full model with all potential individual-level correlates described above and data for 58 countries (i.e., those with no missing data in any covariate). Models were adjusted by a country and a year indicator variable to control for potential unobserved heterogeneity between countries and variability over time. The estimated aOR and 95% confidence intervals (CIs) account for individual-level weights.

Additional country fixed-effects multivariable logistic regression models test the impact of HIV public stigma on testing uptake while adjusting for sociodemographic and HIV knowledge characteristics. We fit two models with two different HIV testing outcomes: first, having ever tested for HIV and, second, having tested for HIV during the past 12 months. Models estimated the aOR, including country and year indicators variables and individual-level weights.

Finally, to account for the potential impact of country-level HIV prevalence and income on HIV stigma and HIV testing uptake, we fit pooled logistic regression models with robust standard errors clustered by country. Here, pooled regression models were used to avoid confounding from the effects of country-level predictors with no within-country variability from the effects of the country dummies.

In further models, we assessed robustness to model specification by excluding from the analyses countries with a response rate below 70% on the HIV stigma variable and countries where respondents were only women or only ever-married women and men. Missing data were handled with pairwise deletion. Analyses were carried out using Stata/MP 17.0 [23].

RESULTS

Participants and data characteristics

A total of 1 172 841 individuals were included in the study, representing, when weighted, a population of over 1.6 billion individuals (1 609 558 193) across 64 low- and middle-income countries (Table 1). Response rates for the main outcome on HIV stigma varied from 99.77% (in Rwanda) to 39.01% (in Pakistan), with 87.50% of countries with a response rate of over 70% (data not shown). Response to the main outcome was dependent on the respondent having ever heard of HIV. In countries with a lower prevalence of people having ever heard of HIV, the response rate to questions on HIV stigma was lower. The prevalence of having ever heard of HIV ranged from 56.14% in Pakistan to 99.91% in Belarus. Yet, in 58 countries (90.63% of the countries included in the sample) over 80% of the population had heard of HIV and in 45 countries (70.31% of the countries included in the sample) over 90% of the population had heard of HIV.

Prevalence estimates of HIV public stigma towards people with HIV

The weighted prevalence of stigmatized and discriminatory attitudes towards people with HIV varied substantially across countries (Figure 1), with a difference of up to 77.71 percentage points between the countries with the highest and lowest prevalence rates (Figure 2). Prevalence ranged from 12.87% (95% CI 12.39–13.35) in Rwanda to 90.58% (95% CI 89.51–91.54) in Samoa.

Overall HIV public stigma towards people with HIV across countries was 42.44% (95% CI 33.97–51.38) (Figure 3). The prevalence of stigmatized attitudes towards people with HIV was lower among people residing in urban areas than in those in rural areas (38.05% [95% CI 28.06–49.16] vs. 46.47% [95% CI 38.14–55.00], respectively; $p = 0.01$), lower among individuals with higher than lower educational levels (29.11% [95% CI 20.43–39.63] vs. 53.85% [95% CI 44.02–63.39], respectively; $p < 0.01$), lower among the richest than among the poorest (34.11% [95% CI 25.29–44.19] vs. 50.83% [95% CI 42.33–59.28], respectively; $p < 0.01$), and lower among those aged 40–49 years than among those aged 15–19 years (41.83% [95% CI 33.06–51.14] vs. 46.93% [95% CI 38.46–55.59], respectively; $p = 0.05$). No difference

TABLE 1 Descriptive statistics of the sample.

Characteristic	Frequency	Percent or mean (SD), unweighted
Total individual-level sample	1 172 841	100%
Total country-level sample	64	100%
HIV stigma		
No/do not know	568 423	48.47%
Yes	604 418	51.53%
Ever taken a test for HIV		
No	605 223	60.54%
Yes	394 566	39.46%
Taken test for HIV past year		
No	812 505	81.30%
Yes	186 861	18.70%
Sex		
Woman	846 685	72.19%
Man	326 156	27.81%
Geographical location		
Urban	487 138	41.95%
Rural	674 118	58.05%
Educational level		
None or pre-primary	274 492	23.47%
Primary	401 215	34.31%
Secondary	312 222	26.70%
Higher	181 524	15.52%
Wealth quintile		
Poorest	213 199	18.18%
Second	229 425	19.56%
Middle	239 090	20.39%
Fourth	241 894	20.62%
Richest	249 233	21.25%
Age group, years		
15–19	215 709	18.39%
20–29	385 564	32.87%
30–39	328 859	28.04%
40–49	242 709	20.69%
Knowledge HIV		
No comprehensive knowledge	922 281	83.26%
Comprehensive knowledge	185 432	16.74%
Year		
2015	10 201	0.87%
2016	95 260	8.12%
2017	196 761	16.78%
2018	247 268	21.08%
2019	392 169	33.44%
2020	147 330	12.56%
2021	83 852	7.15%
GDP per capita 2017 international dollars	1 160 560	7064.176
	(63 countries)	(5272.30)
HIV prevalence	1 083 451	1.42
	(53 countries)	(2.38)

Abbreviation: GDP: gross domestic product; SD: standard deviation.

was observed between men and women in the unadjusted prevalence of HIV public stigma (38.95% [95% CI 31.27–47.21] vs. 43.98% [95% CI 33.69–54.82], respectively; $p = 0.35$).

Sociodemographic determinants of HIV public stigma towards people with HIV and impact on testing uptake

In multivariable logistic regression models, the estimated aOR of HIV stigma (Table 2) showed that men had, on average, lower odds of reporting stigmatized and discriminatory attitudes towards people with HIV than did women (aOR 0.91 [95% CI 0.89–0.92]). There was an inverse, dose–response association between HIV public stigma and educational level, wealth quintile, and age group, whereby higher levels of education (higher education vs. none or pre-primary: aOR 0.41 [95% CI 0.35–0.48]), wealth (richest vs. poorest quintile: aOR 0.54 [95% CI 0.45–0.65]), and age (40–49 vs. 15–19 years: aOR 0.66 [95% CI 0.57–0.75]) were associated with lower odds of holding stigmatized attitudes towards people with HIV. There was a strong association between HIV stigma and knowledge of HIV: individuals with comprehensive knowledge of HIV had lower odds of reporting stigmatized and discriminatory attitudes towards people with HIV (aOR 0.34 [95% CI 0.30–0.38]). No difference in the odds of stigmatized attitudes was observed between individuals residing in rural versus urban areas (aOR 1.03 [95% CI 0.94–1.13]).

Holding stigmatized and discriminatory attitudes towards people with HIV was associated with lower

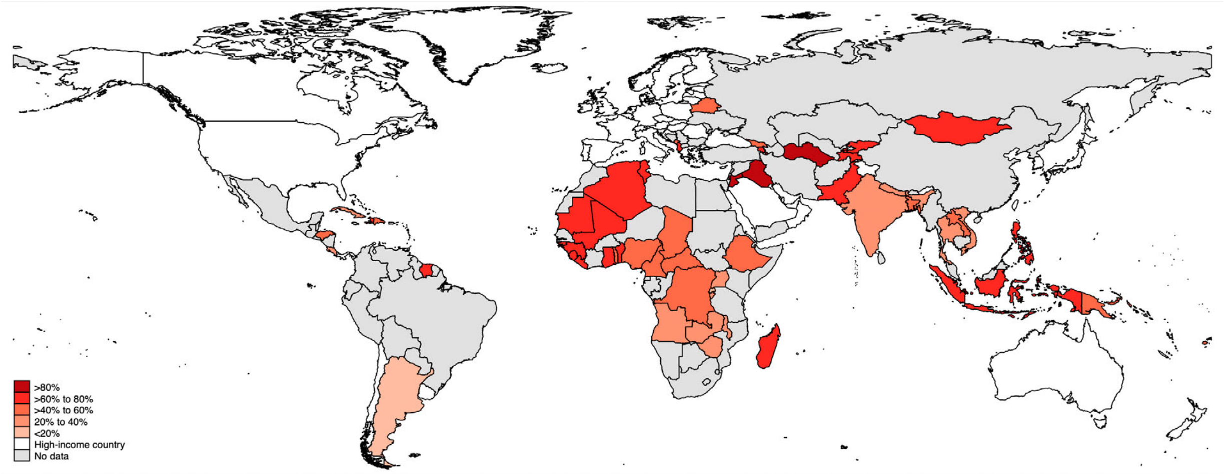

FIGURE 1 Map of prevalence estimates of stigma towards people with HIV among the population aged 15–49 years. Latest available data from 2015 to 2021. *Note*: High-income countries per the World Bank country income classification as of 2021.

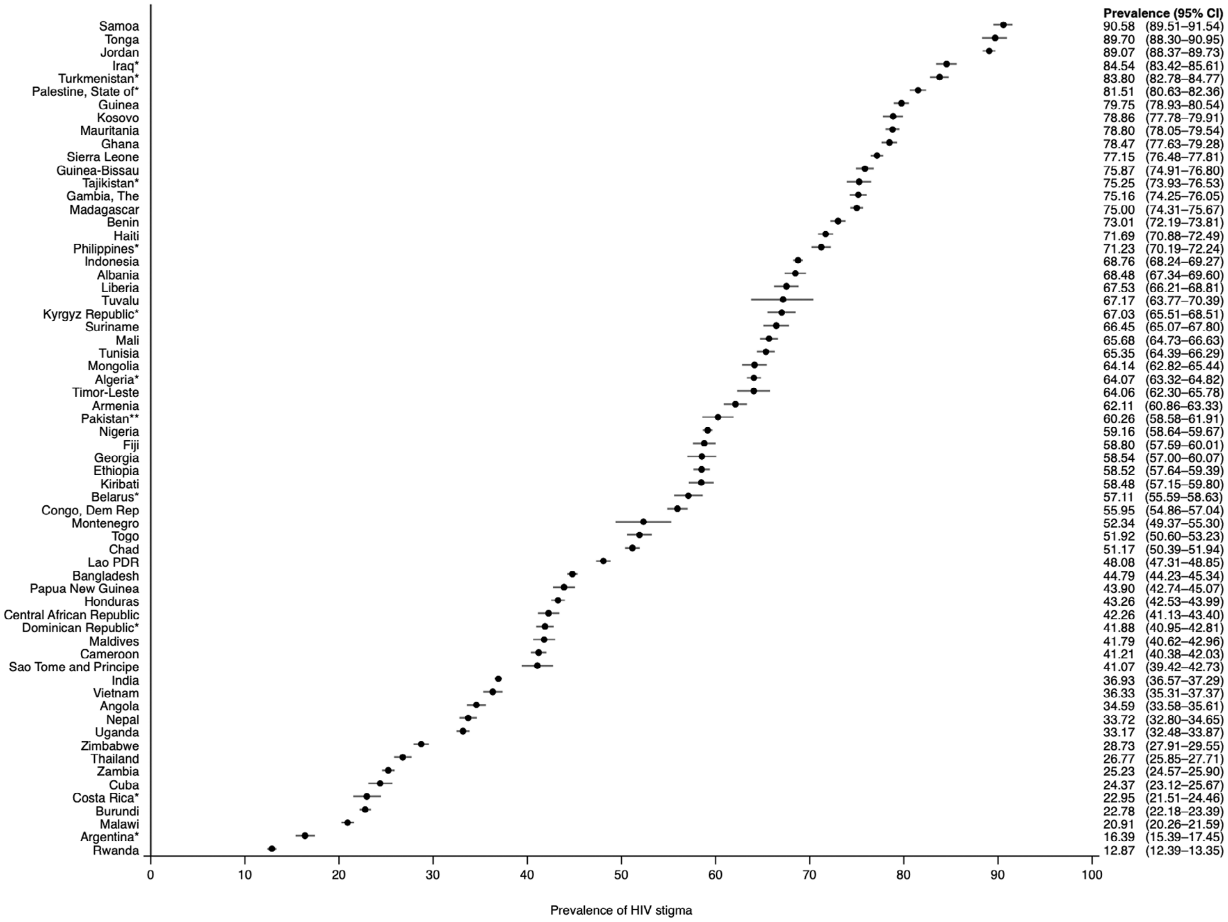

FIGURE 2 Prevalence estimates and 95% confidence intervals (CIs) of stigma towards people with HIV among the population aged 15–49 years. Latest available data from 2015 to 2021. PDR, People's Democratic Republic. *Note*: *The sample only included women. **The sample only included ever-married women and men.

testing uptake (Table 3) after adjusting for the full set of sociodemographic characteristics and HIV knowledge. Stigmatized and discriminatory attitudes were associated with lower odds of having ever tested for HIV (aOR 0.68 [95% CI 0.60–0.76]) and lower odds of having tested for HIV in the last year (aOR 0.77 [95% CI 0.68–0.87]).

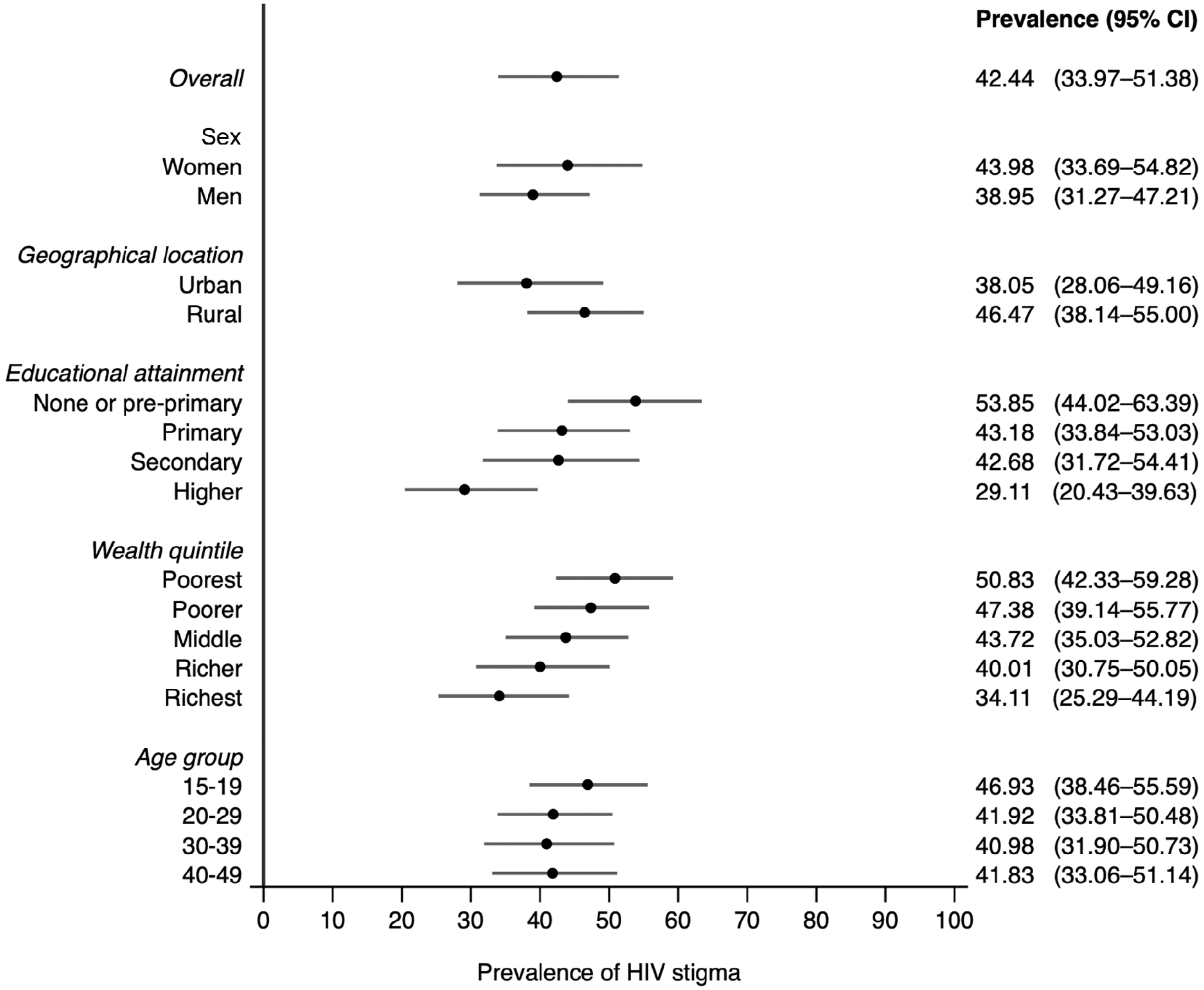

FIGURE 3 Prevalence estimates of stigma towards people with HIV across 64 low- and middle-income countries and by sociodemographic groups. Latest available data from 2015 to 2021. CI, confidence interval.

The odds of HIV public stigma towards people with HIV were, on average, lower among individuals living in either countries with high GDP per capita (aOR 0.93 [95% CI 0.91–0.95]) or high HIV prevalence (aOR 0.85 [95% CI 0.77–0.94]) (Table 4). The association between stigmatized and discriminatory attitudes towards people with HIV and HIV testing uptake did not substantially change when accounting for country income level and HIV prevalence.

Robustness checks

Sensitivity analyses excluding, first, countries ($n = 8$) with a response rate below 70% on the HIV public stigma variable and, second, countries where respondents were only women or only ever-married women and men ($n = 12$) yielded qualitatively similar conclusions to those obtained with the full sample (Appendix A3–A6).

DISCUSSION

In this large cross-sectional study of over 1.1 million individuals in 64 low- and middle-income countries, we found that stigmatized and discriminatory attitudes towards people with HIV were prevalent in all countries, and that the level of HIV public stigma was associated with sociodemographic characteristics. Disadvantaged individuals with lower educational level and wealth were associated with holding greater stigma towards people with HIV, consistent with other findings in low- and middle-income countries [24–31]. Women and adolescents were also associated with having more stigmatized attitudes. Further, holding stigmatized and discriminatory attitudes towards people with HIV was associated with lower HIV testing uptake, which is consistent with previous research [29, 30].

HIV public stigma is present in all countries. However, we observed great differences across countries in

TABLE 2 Sociodemographic characteristics and HIV knowledge as drivers of HIV public stigma across 58 low- and middle-income countries; latest available data from 2015 to 2021.

	HIV stigma	
	aOR	**95% CI**
Sex		
Woman	Reference	
Man	0.91***	0.89–0.92
Geographical location		
Urban	Reference	
Rural	1.03	0.94–1.13
Educational level		
None or pre-primary	Reference	
Primary	0.72***	0.67–0.78
Secondary	0.61***	0.54–0.69
Higher	0.41***	0.35–0.48
Wealth quintile		
Poorest	Reference	
Second	0.90	0.79–1.02
Middle	0.76***	0.66–0.86
Fourth	0.62***	0.54–0.72
Richest	0.54***	0.45–0.65
Age group, years		
15–19	Reference	
20–29	0.88*	0.78–0.99
30–39	0.72***	0.63–0.82
40–49	0.66***	0.57–0.75
Knowledge of HIV		
No comprehensive knowledge	Reference	
Comprehensive knowledge	0.34***	0.30–0.38
Number of individuals	1 092 632	
Number of countries	58	

Note: Constant calculated but not shown; model adjusted by country and year indicator variables; robust standard errors.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

*$p < 0.05$; ***$p < 0.001$.

the prevalence of stigma towards people with HIV, which, coupled with the sociodemographic inequalities in attitudes, may require differing complex approaches to eliminate stigma across settings where it is more entrenched and a focus on populations with greater stigma and discrimination towards people with HIV. This is consistent with the recommendations of a review of interventions for ending HIV stigma that highlighted the need to implement interventions contextualized to the setting and subpopulation [32].

Having no comprehensive knowledge about HIV disease was a key characteristic for reporting stigmatized and discriminatory attitudes towards people with HIV. Lack of knowledge may mean no understanding of the actual reality of HIV, risks, and implications for people with HIV, people affected by HIV, and communities. Thus, interventions for eliminating stigma should focus on increasing knowledge about HIV in individuals and communities, in line with the results of a meta-analysis of the effectiveness of HIV stigma-reducing interventions by increasing HIV knowledge [33]. Yet, some studies argue that information-based approaches and educational interventions alone rarely change negative attitudes but teach people to suppress them [32]. Combined interventions, including personal contact with people with HIV, skills building, counselling and support, and structural and biomedical approaches have seen positive reductions in stigma [32, 34].

In settings with a higher prevalence of HIV, reported stigma is commonly lower. This may be because of a greater likelihood of lived experiences in contact with HIV along with greater knowledge of the disease at the individual and community levels [29, 35]. Interventions for eliminating stigma could include, for example, national- and community-level campaigns, reaching entire populations, as well as campaigns targeting smaller population groups. Interventions could also be included in educational settings to target adolescents, the age group associated with higher levels of stigmatized attitudes.

This study has several strengths. It is the largest study to explore HIV public stigma towards people with HIV in the general population aged 15–49 years, including investigating the association between stigmatized and discriminatory attitudes and sociodemographic characteristics. This study used nationally representative probability samples, compared with previous studies using non-probability samples from people with HIV or healthcare workers. Further, data are comparable among countries because of the common design across nationally implemented MICS or DHS questionnaires. Finally, this is the largest study to investigate the impact of stigma on HIV testing uptake and, in turn, on ending HIV.

However, some limitations warrant consideration. First, measurement errors in the assessment of the main outcome variable may have biased our results in different ways. We used self-reported data, for which response bias could have over- or underestimated the strength of the associations. Reporting bias may have occurred if participants reported answers concealing stigmatized attitudes because of a lack of social acceptability of stigmatized attitudes. This would have biased our estimates towards the null. Estimates could have also been biased in this same direction if stigmatized attitudes were concealed

TABLE 3 HIV public stigma as driver of testing uptake across 53 low- and middle-income countries, latest available data from 2015 to 2021.

	Ever tested for HIV		Tested for HIV past year	
	aOR	**95% CI**	**aOR**	**95% CI**
HIV stigma				
No stigma/do not know	Reference		Reference	
Yes stigma	0.68***	0.60–0.76	0.77***	0.68–0.87
Sex				
Woman	Reference		Reference	
Man	0.38***	0.36–0.39	0.61***	0.60–0.63
Geographical location				
Urban	Reference		Reference	
Rural	0.73***	0.65–0.82	0.76***	0.66–0.87
Educational level				
None or pre-primary	Reference		Reference	
Primary	1.91***	1.72–2.12	1.50***	1.33–1.70
Secondary	2.29***	1.96–2.68	1.67***	1.38–2.03
Higher	1.79***	1.47–2.18	1.75***	1.37–2.25
Wealth quintile				
Poorest	Reference		Reference	
Second	0.87	0.75–1.00	0.91	0.75–1.11
Middle	0.82*	0.70–0.96	0.87	0.72–1.05
Fourth	0.71***	0.59–0.84	0.88	0.72–1.08
Richest	0.81*	0.66–0.99	0.79	0.61–1.01
Age group, years				
15–19	Reference		Reference	
20–29	9.87***	8.43–11.56	3.59***	3.0–4.21
30–39	21.37***	18.09–25.24	3.29***	2.79–3.88
40–49	11.95***	10.06–14.20	1.71***	1.41–2.08
Knowledge of HIV				
No comprehensive knowledge	Reference		Reference	
Comprehensive knowledge	1.34***	1.16–1.55	1.02	0.87–1.19
Number of individuals	938 537		938 163	
Number of countries	53		53	

Note: Constant calculated but not shown; model adjusted by country and year indicator variables; robust standards errors.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

*$p < 0.05$.***$p < 0.001$.

under the responses reporting doubt ('don't know/not sure/it depends'), which we did not classify as HIV public stigma towards people with HIV to ensure the outcome variable could capture well-defined stigmatized and discriminatory attitudes. Stigma and discrimination is complex to measure as they are a compound of beliefs, attitudes, and behaviours. Here, given the dearth of data and the complexity of measuring this social reality, we used the approach taken by UNAIDS [19].

Second, measurement errors may also have occurred in other aspects of this study. For example, because some country questionnaires (mostly with older surveys) used 'AIDS' instead of 'HIV' and referred to 'students' instead of 'children attending school', measurement bias may have affected comparability in unknown directions. We included in the models a year indicator variable that could have helped control for this variability over time. Recall bias could have occurred with testing for HIV,

TABLE 4 Country-level determinants (gross domestic product [GDP] and prevalence of HIV) of HIV public stigma and testing uptake across 48 low- and middle-income countries; latest available data from 2015 to 2021.

	HIV stigma		Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
HIV stigma						
No stigma/do not know			Reference		Reference	
Yes stigma			0.66***	0.58–0.75	0.74***	0.66–0.83
GDP per capita 2017 international dollars (PPP) (in thousands)	0.93***	0.91–0.95	1.03*	1.00–1.05	0.97***	0.95–0.98
HIV prevalence	0.85**	0.77–0.94	1.71***	1.30–2.26	1.37***	1.24–1.51
Number of individuals	1 020 724		884 101		883 767	
Number of countries	48		45		45	

Note: All models are adjusted for sex, geographical location, educational level, wealth quintile, age group, and knowledge of HIV. Constant calculated but not shown; robust standard errors clustered by country.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; PPP, purchasing power parity.

p* < 0.05.*p* < 0.01.****p* < 0.001.

where individuals do not remember or were not aware of having been tested for HIV, thus misclassifying individuals because of measurement error. This would have biased our estimates towards overestimating associations between the predictors and the HIV testing outcomes. Also, the index measuring knowledge on HIV could have included other variables measuring other aspects of the HIV continuum of care, such as knowledge of antiretroviral drugs for treatment as prevention. However, more variables were not available to be included to allow cross-national comparability, and, as such, this index is a proxy based on the best available data. Further, measurement error is likely to have also occurred for capturing the respondents' gender as DHS and MICS measure these in a binary manner, ignoring within this variable non-binary individuals and trans men and women.

Third, HIV prevalence was measured nationally instead of at the community level, where the impact on attitudes may be stronger. Measurement at a higher level may pose a risk of ecological fallacy, as – within countries – it is possible that individuals reporting higher levels of stigma may have life experiences in communities with a lower prevalence of HIV. Fourth, some countries had very low response rates mostly because respondents reported never having heard of HIV. We excluded these countries in sensitivity analyses to ensure the robustness of the results and found no qualitative changes in the results. Finally, we were unable to explore the effects of other factors that could potentially be important determinants of holding stigmatized and discriminatory attitudes towards people with HIV, such as religion, age other than 15–49 years, race, ethnicity, or the role of structural and institutional discrimination arising, for example, from government-supported policies or collective discourses, such as the mass media, among others. In this study, we focused solely on measuring stigma towards people with HIV. Further studies could attempt to measure the aforementioned factors not included in this study as well as intersectional stigma and its impact on engagement with other stages of the HIV care continuum and health-related quality of life.

In conclusion, this multi-national cross-sectional study found that stigmatized and discriminatory attitudes towards people with HIV exist in all countries, with great variation among them. Attitudes varied by sociodemographic characteristics, with individuals with less education and wealth, women, and adolescents showing more negative attitudes towards people with HIV. Importantly, we found that these attitudes were linked to lower HIV testing uptake, which provides evidence that stigmatized and discriminatory attitudes are barriers to ending HIV and highlights the importance of addressing stigma and discrimination towards people with HIV. Variability in attitudes across countries and sociodemographic characteristics shows the need to design interventions for reducing stigma towards people with HIV that are contextualized to the setting and subpopulation.

AUTHOR CONTRIBUTIONS

Ana Mendez-Lopez conceptualized the study and methodology, analysed the data, and wrote the first draft. All authors reviewed the study and edited the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests related to this work. Jeffrey V. Lazarus is the co-chair of HIV Outcomes and a member of the Board of Directors of SHARE Global Health Foundation. He has received funding to ISGlobal from AbbVie, Gilead Sciences, MSD, and Roche Diagnostics.

DATA AVAILABILITY STATEMENT

This study is based on publicly available microdata that can be accessed through the MICS and DHS websites upon registration and request. Country data are readily available from the websites of the World Bank Development Indicators database and the United Nations Population Fund population estimates database.

ETHICS COMMITTEE APPROVAL

This study employed secondary public data and needed no ethics committee approval.

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REFERENCES

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). *HIV and Stigma and Discrimination*. UNAIDS; 2021.
2. Joint United Nations Programme on HIV/AIDS (UNAIDS). Global AIDS Strategy 2021–2026. End Iinequalities. End AIDS. Switzerland: UNAIDS. 2021. Accessed July, 2023. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf
3. World Health Organization. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022–2030. 2022. Accessed July, 2023. https://www.who.int/publications/i/item/9789240053779
4. Stover J, Glaubius R, Teng Y, et al. Modeling the epidemiological impact of the UNAIDS 2025 targets to end AIDS as a public health threat by 2030. *PLoS Med*. 2021;18(10):e1003831. doi:10.1371/journal.pmed.1003831
5. Parker R, Aggleton P. HIV and AIDS-related stigma and discrimination: a conceptual framework and implications for action. *Soc Sci Med*. 2003;57(1):13-24. doi:10.1016/S0277-9536(02)00304-0
6. Earnshaw VA, Chaudoir SR. From conceptualizing to measuring HIV stigma: a review of HIV stigma mechanism measures. *AIDS Behav*. 2009;13(6):1160-1177.
7. Mahajan AP, Sayles JN, Patel VA, et al. Stigma in the HIV/-AIDS epidemic: a review of the literature and recommendations for the way forward. *AIDS*. 2008;22:S67-S79. doi:10.1097/01.aids.0000327438.13291.62
8. Musheke M, Ntalasha H, Gari S, et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in sub-Saharan Africa. *BMC Public Health*. 2013;13(1):1-16.
9. Ahmed S, Autrey J, Katz IT, et al. Why do people living with HIV not initiate treatment? A systematic review of qualitative evidence from low-and middle-income countries. *Soc Sci Med*. 2018;213:72-84. doi:10.1016/j.socscimed.2018.05.048
10. Katz IT, Ryu AE, Onuegbu AG, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. *J Int AIDS Soc*. 2013;16:18640.
11. Rueda S, Mitra S, Chen S, et al. Examining the associations between HIV-related stigma and health outcomes in people living with HIV/AIDS: a series of meta-analyses. *BMJ Open*. 2016;6(7):e011453. doi:10.1136/bmjopen-2016-011453
12. Lazarus JV, Safreed-Harmon K, Barton SE, et al. Beyond viral suppression of HIV—the new quality of life frontier. *BMC Med*. 2016;14(1):94.
13. Safreed-Harmon K, Anderson J, Azzopardi-Muscat N, et al. Reorienting health systems to care for people with HIV beyond viral suppression. *Lancet HIV*. 2019;6(12):e869-e877. doi:10.1016/S2352-3018(19)30334-0
14. Lazarus JV, Safreed-Harmon K, Kamarulzaman A, et al. Consensus statement on the role of health systems in advancing the long-term well-being of people living with HIV. *Nat Commun*. 2021;12(1):4450.
15. Logie C, Gadalla TM. Meta-analysis of health and demographic correlates of stigma towards people living with HIV. *AIDS Care*. 2009;21(6):742-753. doi:10.1080/09540120802511877
16. Lazarus JV, Wohl DA, Cascio M, et al. Long-term success for people living with HIV: a framework to guide practice. *HIV Med*. 2023;24(suppl 2):8-19.
17. USAID. *Demographic and Health Survey*. USAID; 2023.
18. The World Bank Group. World Bank Country and Lending Groups. 2023. Accessed January, 2023. https://dhsprogram.com/
19. UNAIDS. Global AIDS monitoring 2023 Indicators and questions for monitoring progress on the 2021 Political Declaration on HIV and AIDS. Switzerland, Geneva: UNAIDS. 2022.
20. Croft TN, Marshall AM, Allen CK, Arnold F, Assaf S, Balian S. *Guide to DHS Statistics*. ICF; 2018:645.
21. The World Bank Group. *World Development Indicators DataBank*. The World Bank Group; 2022.
22. United Nations Population Division. *World Population Prospects 2019*. United Nations Population Division Department of Economic and Social Affairs; 2022.
23. StataCorp. *Stata Statistical Software: Release 17*. StataCorp LP; 2021.
24. Chan BT, Tsai AC. HIV stigma trends in the general population during antiretroviral treatment expansion: analysis of 31 countries in sub-Saharan Africa, 2003-2013. *J Acquir Immune Defic Syndr*. 2016;72(5):558-564.
25. Chautrakarn S, Ong-Artborirak P, Naksen W, et al. Stigmatizing and discriminatory attitudes toward people living with HIV/AIDS (PLWHA) among general adult population: the results from the 6(th) Thai National Health Examination Survey (NHES VI). *J Glob Health*. 2023;13:04006.
26. Iqbal S, Maqsood S, Zafar A, Zakar R, Zakar MZ, Fischer F. Determinants of overall knowledge of and attitudes towards HIV/AIDS transmission among ever-married women in Pakistan: evidence from the demographic and health survey 2012-13. *BMC Public Health*. 2019;19(1):793.

27. Li X, Yuan L, Li X, et al. Factors associated with stigma attitude towards people living with HIV among general individuals in Heilongjiang, Northeast China. *BMC Infect Dis*. 2017;17(1):154.
28. Suantari D. Misconceptions and stigma against people living with HIV/AIDS: a cross-sectional study from the 2017 Indonesia demographic and health survey. *Epidemiol Health*. 2021;43:e2021094. doi:10.4178/epih.e2021094
29. Genberg BL, Hlavka Z, Konda KA, et al. A comparison of HIV/AIDS-related stigma in four countries: negative attitudes and perceived acts of discrimination towards people living with HIV/AIDS. *Soc Sci Med*. 2009;68(12):2279-2287. doi:10.1016/j.socscimed.2009.04.005
30. Kalichman SC, Shkembi B, Wanyenze RK, et al. Perceived HIV stigma and HIV testing among men and women in rural Uganda: a population-based study. *Lancet HIV*. 2020;7(12):e817-e824. doi:10.1016/S2352-3018(20)30198-3
31. Teshale AB, Tesema GA. Discriminatory attitude towards people living with HIV/AIDS and its associated factors among adult population in 15 sub-Saharan African nations. *PloS One*. 2022;17(2):e0261978. doi:10.1371/journal.pone.0261978
32. Andersson GZ, Reinius M, Eriksson LE, et al. Stigma reduction interventions in people living with HIV to improve health-related quality of life. *Lancet HIV*. 2020;7(2):e129-e140. doi:10.1016/S2352-3018(19)30343-1
33. Mak WWS, Mo PKH, Ma GYK, Lam MYY. Meta-analysis and systematic review of studies on the effectiveness of HIV stigma reduction programs. *Soc Sci Med*. 2017;188:30-40. doi:10.1016/j.socscimed.2017.06.045
34. Stangl AL, Lloyd JK, Brady LM, Holland CE, Baral S. A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come? *J Int AIDS Soc*. 2013;16(3 suppl 2):18734.
35. Chan BT, Tsai AC. Personal contact with HIV-positive persons is associated with reduced HIV-related stigma: cross-sectional analysis of general population surveys from 26 countries in sub-Saharan Africa. *J Int AIDS Soc*. 2017;20(1):21395.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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2.4 Study 4: Population uptake and effectiveness of test-and-treat antiretroviral therapy guidelines for preventing the global spread of HIV: an ecological cross-national analysis

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ORIGINAL RESEARCH

Population uptake and effectiveness of test-and-treat antiretroviral therapy guidelines for preventing the global spread of HIV: an ecological cross-national analysis

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Objectives

Although the benefits of adopting test-and-treat antiretroviral therapy (ART) guidelines that recommend initiation of ART regardless of CD4 cell counts have been demonstrated at the individual level, there is uncertainty about how this translates to the population level. Here, we explored whether adopting ART guidelines recommending earlier treatment initiation improves population ART access and viral suppression and reduces overall disease transmission.

Methods

Data on ART initiation guidelines and treatment coverage, viral suppression, and HIV incidence from 37 European and Central Asian countries were collected from the European Centre for Disease Prevention and Control and the Global HIV Policy Watch and HIV 90-90-90 Watch databases. We used multivariate linear regression models to quantify the association of ART initiation guidelines with population ART access, viral suppression, and HIV incidence, adjusting for potential confounding factors.

Results

Test-and-treat policies were associated with 15.2 percentage points (pp) [95% confidence interval (CI) 0.8–29.6 pp; $P = 0.039$] greater treatment coverage (proportion of HIV-positive people on ART) compared with countries with ART initiation at CD4 cell counts ≤ 350 cells/μL. The presence of test-and-treat policies was associated with 15.8 pp (95% CI 2.4–29.1 pp; $P = 0.023$) higher viral suppression rates (people on ART virally suppressed) compared with countries with treatment initiation at CD4 counts ≤ 350 cells/μL. ART initiation at CD4 counts ≤ 500 cells/μL did not significantly improve ART coverage compared to initiation at CD4 counts ≤ 350 cells/μL but achieved similar degrees of viral suppression as test-and-treat.

Conclusions

Test-and-treat was found to be associated with substantial improvements in population-level access to ART and viral suppression, further strengthening evidence that rapid initiation of treatment will help curb the spread of HIV.

Keywords: ecological, health systems, HIV care continuum, structural drivers, test-and-treat

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Introduction

In 2015, the World Health Organization (WHO) and the European AIDS Clinical Society called for universal test-and-treat programmes, with initiation of antiretroviral therapy (ART) immediately upon diagnosis of HIV infection, as a means to reduce rates of HIV-related illness and mortality and onward transmission [1–3]. The rationale for reducing

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onward transmission derived primarily from evidence that early treatment reduced the risk of mother-to-child transmission and in serodiscordant couples [4–16]. The HIV Prevention Trials Network (HPTN052) trial had found that ART initiation at CD4 counts of between 350 and 550 cells/μL led to a reduction of 96% in HIV transmission compared to delaying ART initiation until the CD4 count was ≤ 250 cells/μL [12,16]. This was consistent with earlier observational studies and supported by systematic reviews [11,13,14,17]. Yet, the argument that this would lead to population-level benefits was controversial. Some argued that expanding ART might create a false sense of security among those affected, perversely encouraging greater rates of unsafe sex [18–20], which has been contested [21–24]. Others highlighted constraints to scaling up treatment as a result of limited resources, especially in low-income settings [25–27], uncertainty about the use of data from clinical trials that showed 'modest benefits' [28], nonreplicability at the community level [29,30], and the risk of increasing rates of adverse effects caused by ART and resistance [26,31].

In Europe, a key argument centred on whether findings in couples could be generalized to the wider population, especially as the incidence was lower than in other parts of the world and, in many European countries, was declining. This reflected the limited evidence at the population level, with studies producing mixed findings but often suggesting that population-level benefits may be more modest than those found in trials at the individual level. A number of ecological studies have been carried out, but mostly in single communities. An association between greater ART coverage and lower viral loads and transmission has been reported in diverse settings, including British Columbia in Canada [32–34], San Francisco in the USA [35], KwaZulu-Natal in South Africa [17,36], and Taiwan [37]. One cross-national study found that expanding ART coverage in the 30 highest AIDS mortality burden countries correlated with reduced mortality rates from HIV-related causes [38]. However, a recent review argued that findings from existing population-level studies were mixed, with one study reporting decreasing risk per contact among those on ART being counteracted by more unsafe sexual episodes [18]. Another review found that test-and-treat appeared to be less effective at the population level than anticipated from modelling studies [29,30].

Here, we take advantage of a unique opportunity to test the impact of the expansion of test-and-treat policies in 37 European and Central Asian countries. Several countries pre-empted the adoption of the test-and-treat guidelines in WHO's 2015 recommendations, while others have yet to change (see Table S1). These marked differences in timing enabled us to test the hypothesis that expanding test-and-treat guidelines increases population access to ART coverage and, in so doing, improves viral suppression and reduces HIV incidence (as described in Fig. 1).

Methods

Data sources

We collected data on the prevalence of HIV-positive status, the proportion of people diagnosed with HIV infection with access to ART, and proportion of people on ART with viral suppression from the European Centre for Disease Prevention and Control (ECDC)'s *HIV Treatment and Care* and *Continuum of HIV Care* reports covering 37 countries in the WHO European Region [39,40]. This includes the European Union and European Economic Area (EU/EEA) (24 countries) as well as Eastern European and Central Asian countries (13 countries). ECDC's system for monitoring progress against the Dublin Declaration on Partnership to Fight HIV/AIDS has been described elsewhere [39–42]; briefly, ECDC surveys health ministries and other health authorities for data on access to ART and viral suppression. The years for which data are available vary across countries between 2012 and 2016, with most (26 countries) providing data for the year 2015. Table S2 lists all 37 countries included in the analyses and details the year of available data for each country. The data sources also varied across countries [39]. For instance, for the number of people with HIV infection who are on ART, 29% of countries used surveillance data, 26% used cohort data,

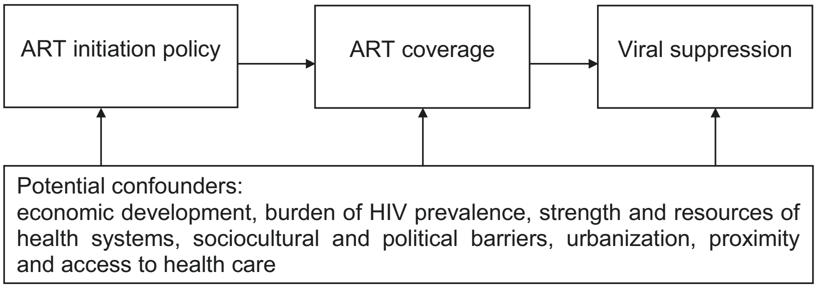

Fig. 1 Conceptual framework of the relationship between antiretroviral therapy (ART) initiation policies, ART coverage and viral suppression.

and 45% used another data source. For reporting the number of people who are virally suppressed, 26% of countries used surveillance data, 44% used cohort data, and 30% used another data source. Table S3 provides detailed information of the data source used in each country.

The European Centre for Disease Prevention and Control has produced definitions to harmonize reporting practices [41]. Current ART status is based on persons using ART, irrespective of treatment regimen or treatment interruptions and discontinuations. Viral suppression is defined as having initiated treatment and achieved a viral load ≤ 200 HIV-1 RNA copies/mL of blood at the last attendance for HIV care. Nonetheless, countries employed slightly varying definitions for reporting data on ART prevalence and viral suppression, introducing measurement errors [41–43]. Data on access to ART and viral suppression in Kazakhstan and Kyrgyzstan only included patients who were ≥ 15 years old.

Data on new HIV infection rates per 100 000 population were obtained for all countries from The European Surveillance System (TESSy) to which countries provide surveillance data, as reported by ECDC and the WHO Regional Office for Europe [44]. To capture changes in HIV transmission, we calculated the growth rate as the difference between the rate in the year for which each country had available data on the other variables (ART access and viral suppression) and the rate in the previous year. However, these data have limits in capturing reduced HIV transmission, as newly reported HIV diagnoses include recently infected individuals as well as those who were infected several years ago but only recently tested for HIV [44].

Data on ART guidelines in the year for which the data were available were taken from the ECDC Dublin Declaration monitoring and country reports [40,45,46], the Global HIV Policy Watch database (June 2017 edition) [47], and the HIV 90-90-90 Watch database (May 2017 edition) [48]. Table S1 summarizes the ART policies that countries had in place in the year for which the HIV data were available. Where discrepancies occurred, we used the more comprehensive HIV Policy Watch database. Guidelines were categorized into three groups: those recommending ART initiation at CD4 cell counts ≤ 350 cells/μL, ART initiation at CD4 counts ≤ 500 cells/μL, and universal treatment (i.e. test-and-treat or treatment initiation irrespective of CD4 count). No country in the sample used the 2003 WHO HIV treatment guidelines recommending treatment initiation at CD4 counts ≤ 200 cells/μL.

Statistical modelling

To adjust for potential confounding factors, we used multivariate linear regression models, corresponding to the causal chain outlined in Figure 1:

$$\begin{aligned}&\text{Prevalence of HIV-positive persons with ART access}_i\\&\quad= \alpha + \beta_1\,\text{ART guidelines}_i + \beta_2 \log \text{GDP}_i\\&\qquad+ \beta_3\,\text{public health expenditure}_i\\&\qquad+ \beta_4\,\text{HIV prevalence}_i + \beta_5\,\text{region} + \varepsilon_i\end{aligned}$$

Here, i is country, GDP is gross domestic product per capita and ε is the error term. ART guideline is coded as an ordinal variable, as described above. Log GDP per capita is in international constant 2011 purchasing power parity-adjusted US dollars to facilitate cross-national comparisons and adjust for positive skew. To address the possibility that wealthier nations may achieve greater access, we also adjusted for public health expenditures per capita in international constant 2011 US dollars adjusted for purchasing power parity and inflation. We also included additional adjustments for country HIV burden and region (EU/EEA or Eastern Europe and Central Asia). Data on the number of people with HIV infection were taken from ECDC [39] and data on the total population were taken from the World Bank World Development Indicators (WDI) database to calculate HIV prevalence. All other data on control variables were taken from the World Bank WDI database for the year 2015, corresponding to the year in which most countries reported HIV data, except for public health expenditures, which were from 2014, the latest year in which all countries provided data [49].

In the second step, we quantified the association between ART initiation policy and viral suppression, performing a mediation analysis, as follows:

$$\begin{aligned}&\text{Prevalence of HIV-positive persons with viral}\\&\text{suppression}_i = \alpha + \beta_1\,\text{ART guidelines}_i + \beta_2 \log \text{GDP}_i\\&\qquad+ \beta_3\,\text{public health expenditure}_i\\&\qquad+ \beta_4\,\text{HIV prevalence}_i + \beta_5\,\text{region} + \varepsilon_i\end{aligned}$$

Finally, we investigated the association between ART initiation guidelines and the growth rate of new HIV infections per 100 000 population as a proxy for change in transmissibility:

$$\begin{aligned}&\text{Growth rate of HIV incidence per 100 000}_i\\&\quad= \alpha + \beta_1\,\text{ART guidelines}_i + \beta_2 \log \text{GDP}_i\\&\qquad+ \beta_3\,\text{public health expenditure}_i\\&\qquad+ \beta_4\,\text{HIV prevalence}_i + \beta_5\,\text{region} + \varepsilon_i\end{aligned}$$

To account for potential heteroscedasticity, robust standard errors were used. In view of the small sample size and potential overfitting, we present for both models, first, unadjusted, more parsimonious results, and, secondly, fully specific models adjusted for several controls. All models were estimated using STATA, version 13.0 (StataCorp, College Station, TX).

Results

Impact of test-and-treat guidelines on population-level ART access among people with diagnosed HIV infection

An estimated 1.2 million people were living with HIV, of whom 0.7 million were receiving ART (< 60%). In the EU/EEA (24 countries), 77.5% of the people diagnosed with HIV infection were on ART and, of those, 86.6% had attained viral suppression. These estimates, respectively, were lower, at 57.1% and 59.8%, in Eastern Europe and Central Asia (13 countries). Table S4 describes the HIV data obtained from the 37 countries in the sample.

At the time the data were published, in April 2017, 14 of the 37 countries had yet to adopt test-and-treat guidelines, which corresponds to about 25% of the population in the 37 countries not covered by universal HIV treatment. We observed that seven countries (all from EU/EEA) began test-and-treat prior to the WHO 2015 guideline update, corresponding to about 20% of the countries included in the sample and covering 35% of the population in the sample countries. Of the 14 countries that have not updated their guidelines to the latest (2015) WHO and EACS recommendations at the time the data were published in 2017, 11 (29.7% of the countries and about 21% of the total population in the sample countries) had guidelines recommending treatment at CD4 cell counts ≤ 500 cells/μL, corresponding to the WHO guidelines of 2013. The guidelines of three countries (Azerbaijan, Lithuania and Tajikistan; 8.1% of the countries and 4% of the sample population) recommend initiation of ART at CD4 cell counts ≤ 350 cells/μL, corresponding to the 2010 WHO guidelines. Of the 14 countries that have not adopted test-and-treat, four countries are from the EU/EEA: Belgium, Bulgaria and Luxemburg (CD4 count ≤ 500 cells/μL), and Lithuania (CD4 count ≤ 350 cells/μL). Table S3 summarizes the state of the ART policies for the studied countries.

Figure 2a (panel 1) shows the proportion of people on ART out of all people living with diagnosed HIV infection by country. Unadjusted, test-and-treat policies achieve greater access to ART (mean 82.4%), compared with policies that employ CD4 threshold restrictions (mean 60.1%). Countries with test-and-treat policies had, on average, 22.3 percentage points more diagnosed HIV-positive people on ART (two-tailed t-test: $t = 4.03$; $P = 0.0003$). As shown in Figure 2b, an increase in access to ART appeared to occur most often when moving from any CD4 restriction to test-and-treat, rather than from the threshold of CD4 count ≤ 350 cells/μL to CD4 count ≤ 500 cells/μL. Table S2 describes the ART initiation guidelines in the year data were available in each of the countries shown in Figure 2a.

Table 1 shows the results of our multivariate linear regression model quantifying the association of test-and-treat with population-level access to ART among people with diagnosed HIV infection. Countries that had test-and-treat policies had a 20.8 (95% CI 5.2–36.4; $P = 0.01$) percentage points increase of people on ART compared with countries with guidelines recommending treatment initiation at CD4 counts ≤ 350 cells/μL. After controlling for the level of economic development, HIV prevalence, subregion and public health care expenditure, the estimated effect size was attenuated to 15.2 percentage points (95% CI 0.8–29.6; $P = 0.039$), appearing to reflect mainly how better resourced and wealthier health systems also achieved higher rates of uptake.

Impact of test-and-treat on population-level viral suppression among people on ART

Figure 3 depicts the positive unadjusted association between the percentage of people diagnosed with HIV infection who were on ART and the percentage of people diagnosed with HIV who were on ART with viral suppression ($r = 0.57$; $P = 0.001$). It shows that countries with higher ART coverage were more likely to achieve a higher percentage of population-level viral suppression among people on ART.

As shown in the unadjusted plots in Figure 4a (panel 2), we observed that test-and-treat policies were associated with a higher proportion of population-level viral suppression among HIV-positive patients on ART (mean 86.1%) compared with countries with CD4 restrictions for ART initiation (mean 67.9%). Countries with ART policies offering treatment for all had, on average, 18.1 percentage points more viral suppression among patients on ART compared with countries restricting treatment only to patients with low CD4 cell counts; this difference was significant at the 5% level (two-sample t-test: $t = 2.91$; $P < 0.007$). Figure 4b shows a steady increase in the average percentage of people on ART with viral suppression as the inclusiveness of the three ART initiation policies increased, whereby, in countries with the most inclusive treatment guidelines, i.e. test-and-treat, the populations achieved the highest levels of viral suppression.

After adjusting for potential confounders in a multivariate linear regression model, as shown in Table 2, we found that test-and-treat was associated with 15.8 percentage points more of people on ART achieving viral suppression compared with countries with treatment initiation at CD4

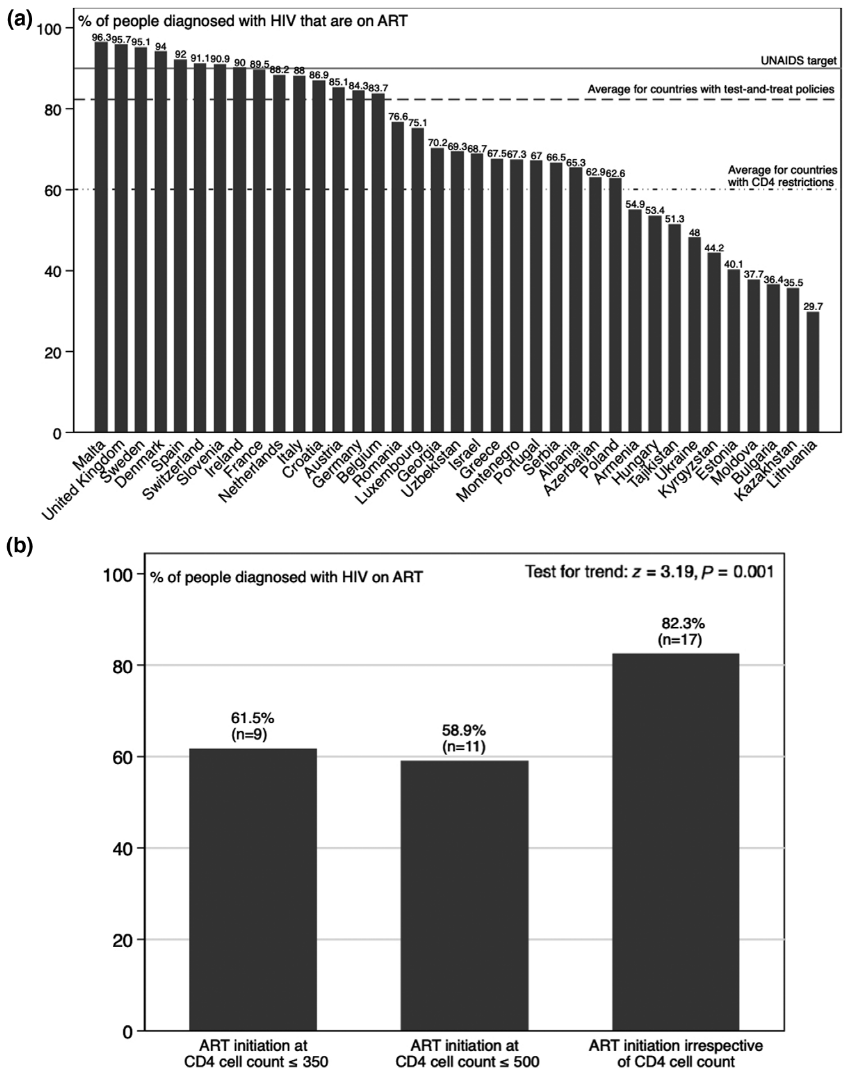

Fig. 2 Population-level access to antiretroviral therapy (ART) and ART initiation guidelines. (a) Percentage of people diagnosed with HIV infection on ART by country and average percentage by ART initiation policy. (b) Percentage of people diagnosed with HIV infection on ART by ART initiation policy.

counts ≤ 350 cells/μL (95% CI 2.4–29.1%; $P = 0.007$). Countries with guidelines recommending initiation of ART at CD4 cell counts ≤ 500 cells/μL achieved similar levels of viral suppression to countries with test-and-treat policies (15.1 percentage points; 95% CI 1.2–29.1; $P = 0.023$).

Impact of test-and-treat on HIV transmission

Table 3 shows the results of our multivariate linear regression model quantifying the association of ART initiation guidelines and the growth rate of new HIV infections per 100 000 population. We found that, after adjusting for potential confounders, countries with ART initiation at CD4 cell counts ≤ 500 cells/μL had an associated 16% reduction in their new HIV infection rates per 100 000, compared with countries with ART initiation at CD4 cell counts ≤ 350 cells/μL (95% CI −30 to −1.4%; $P = 0.033$). No difference was observed between countries with test-and-treat ART guidelines and countries with ART initiation at CD4 cell counts ≤ 350 cells/μL (−6.3%; 95% CI −23.5 to 10.9%; $P = 0.46$).

Robustness check

As country-years of data availability varied, we also included a variable for the year of data availability to

Table 1 Association of antiretroviral therapy (ART) initiation guidelines with population-level access to ART among people diagnosed with HIV infection

	Percentage of people diagnosed with HIV infection on ART	
	Model 1	**Model 2**
ART initiation guidelines		
Initiation at CD4 count ≤ 350 cells/μL	Reference	Reference
Initiation at CD4 count ≤ 500 cells/μL	−2.65 (−19.1 to 13.8)	0.23 (−13.3 to 13.8)
Initiation at any CD4 count (test-and-treat)	20.8* (5.20–36.4)	15.2* (0.82–29.6)
Per 1% increase in GDP per capita (≈$927)		1.58 (−7.89 to 11.1)
Per $1000 increase in health care expenditure per capita		6.55* (1.61–11.5)
Per 1 SD increase in HIV prevalence (SD = 0.17%)		−4.77 (−10.6 to 1.03)
Region		
EU/EEA		Reference
Eastern Europe and Central Asia		3.04 (−14.7 to 20.8)
Number of countries	37	37
R^2	0.319	0.626

A constant was included in all models but is not shown. 95% confidence intervals are shown in brackets. Model 1: unadjusted; model 2: adjusted for level of economic development, HIV prevalence, subregion and public health care expenditure.
EU/EEA, European Union and European Economic Area; SD, standard deviation.
$^*P < 0.05$.

adjust for the potential effect of secular trends. None of the results was qualitatively unchanged.

Discussion

We found a significant association between adoption of test-and-treat guidelines and greater access to both ART and viral suppression compared with the use of a CD4 count ≤ 350 cells/μL threshold, even after adjusting for potential confounding factors. While we found that test-and-treat was associated with greater access to ART when compared with the most restrictive ART initiation policy (CD4 counts ≤ 350 cells/μL), there were no statistically significant differences between ART initiation at CD4 counts ≤ 500 cells/μL and at CD4 counts ≤ 350 cells/μL. This indicates that the effect of test-and-treat on expanding ART coverage is probably substantial in comparison with any alternative ART initiation policy. We also found that greater viral suppression was achieved with both test-and-treat and ART initiation at CD4 counts ≤ 500 cells/μL compared with ART initiation at CD4 counts ≤ 350 cells/μL, which is important given that this is associated with reduced HIV-related illness, deaths, and transmissibility [35,50]. Community viral load has been proposed as an effective population-level biomarker of HIV burden and as a novel means of assessing the potential impact of

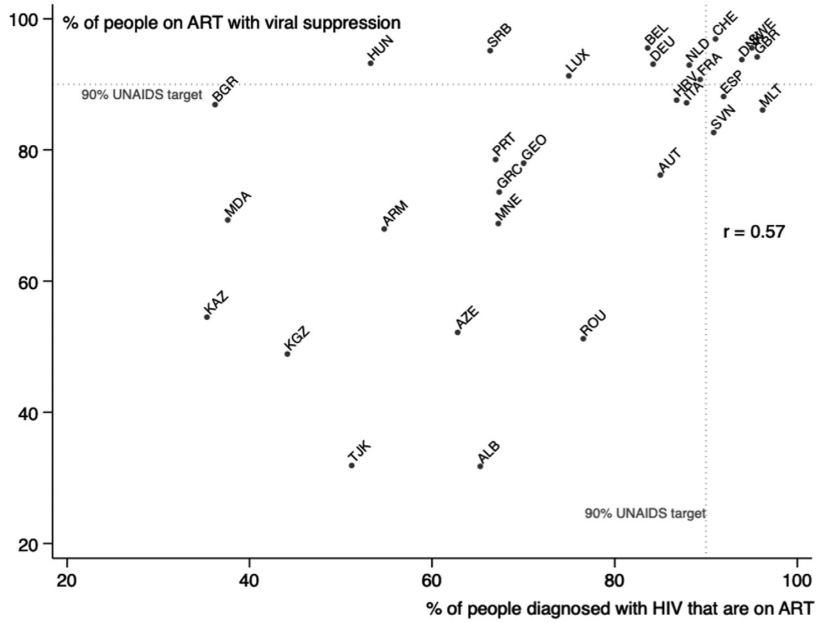

Fig. 3 Association between the percentage of people diagnosed with HIV infection on antiretroviral therapy (ART) and the percentage of people on ART with viral suppression.

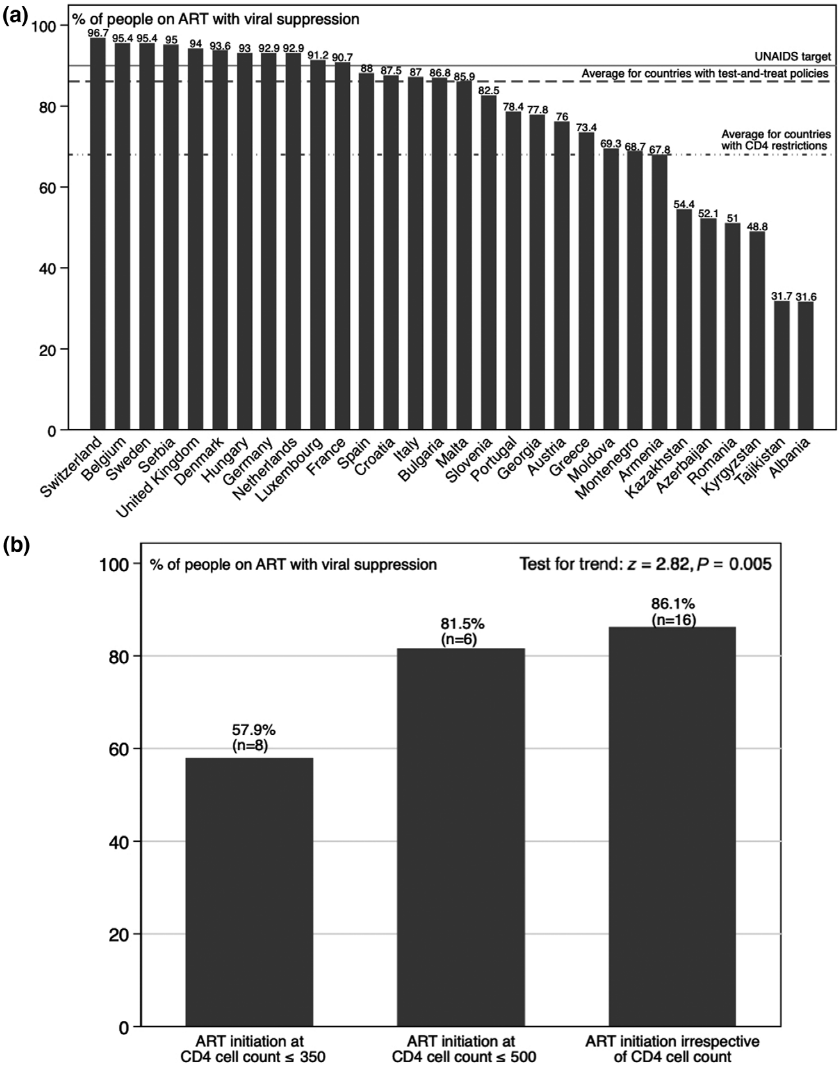

Fig. 4 Population-level viral suppression and antiretroviral therapy (ART) initiation guidelines. (a) Percentage of people on ART with viral suppression by country and average percentage by ART initiation policy. (b) Percentage of people on ART with viral suppression by ART initiation policy.

population-level HIV prevention and treatment interventions [50]. When we studied the association between ART initiation policy and per cent change in new HIV infection rates, we observed that earlier treatment initiation at CD4 counts ≤ 500 cells/μL was associated with a decline in new HIV infections but initiation irrespective of CD4 cell count was not associated with a decline when compared with initiation at CD4 counts ≤ 350 cells/μL.

Our findings are consistent with those of other studies. First, the association between test-and-treat and higher ART coverage is both intuitive and consistent with the findings of other studies showing earlier initiation of ART to be associated with increased ART coverage [51,52]. Secondly, the association between test-and-treat and greater population-level viral suppression among people on ART is also consistent with the results of several studies that reported that increased ART coverage and earlier initiation of ART were linked to improved HIV outcomes [32–34,36–38,52–55], including attainment of viral suppression [35,50,56,57] and reduced transmission and incidence [35,50]. Greater viral suppression of the population under treatment initiation guidelines that recommend therapy for all and for those with higher CD4 cell counts (CD4 counts ≤ 500 cells/μL) might be explained by the steady access to ART that confer these more inclusive policies offering treatment to a greater proportion of the HIV-positive population in contrast to an ART initiation

Table 2 Association of antiretroviral therapy (ART) initiation guidelines with population-level viral suppression among people on ART

	Percentage of people on ART with viral suppression	
	Model 1	Model 2
ART initiation guidelines		
Initiation at CD4 count ≤ 350 cells/μL	Reference	Reference
Initiation at CD4 count ≤ 500 cells/μL	17.6 (−4.06 to 39.3)	15.1* (1.18–29.0)
Initiation at any CD4 count (test-and-treat)	26.9** (7.99–45.9)	15.8* (2.39–29.1)
Per 1% increase in GDP per capita (≈$927)		9.95* (0.71–19.2)
Per $1000 increase in health care expenditure per capita		1.66 (−2.79 to 6.12)
Per 1 SD increase in HIV prevalence (SD = 0.17%)		0.20 (−4.99 to 5.38)
Region		
EU/EEA		Reference
Eastern Europe and Central Asia		−2.71 (−21.4 to 16.0)
Number of countries	30	30
R^2	0.335	0.648

A constant was included in all models but is not shown. 95% confidence intervals are shown in brackets. Model 1: unadjusted; model 2: adjusted for level of economic development, HIV prevalence, subregion and public health care expenditure.
EU/EEA, European Union and European Economic Area; SD, standard deviation.
*$P < 0.05$; **$P < 0.01$.

Table 3 Association of antiretroviral therapy (ART) initiation guidelines with the growth rate of new HIV infections per 100 000 population

	Per cent change in new HIV infection rate per 100 000	
	Model 1	Model 2
ART initiation guidelines		
Initiation at CD4 count ≤ 350 cells/μL	Reference	Reference
Initiation at CD4 count ≤ 500 cells/μL	−17* (−0.30 to −0.043)	−16* (−0.30 to −0.014)
Initiation at any CD4 count (test-and-treat)	−8.2 (−0.21 to 0.043)	−6.3 (−0.24 to 0.11)
Per 1% increase in GDP per capita (≈$927)		−0.031 (−0.095 to 0.033)
Per $1000 increase in health care expenditure per capita		−0.00054 (−0.044 to 0.043)
Per 1 SD increase in HIV prevalence (SD = 0.17%)		−0.025 (−0.053 to 0.0036)
Region		
EU/EEA		Reference
Eastern Europe and Central Asia		−0.013 (−0.18 to 0.16)
Number of countries	36	36
R^2	0.217	0.262

A constant was included in all models but is not shown. 95% confidence intervals are shown in brackets. Model 1: unadjusted; model 2: adjusted for level of economic development, HIV prevalence, subregion and public health care expenditure.
EU/EEA, European Union and European Economic Area; SD, standard deviation.
*$P < 0.05$.

policy that delays treatment initiation until patients reach lower CD4 cell counts.

The apparent effectiveness of test-and-treat in increasing population-level ART coverage among people with diagnosed HIV infection and increasing viral suppression among people on ART reinforces the decision by some countries, beginning in 2011, to adopt ART irrespective of CD4 cell count and immediate initiation of ART with simplified regimens; and it also reinforces the recommendations by the WHO and EACS in 2015 to adopt test-and-treat policies as a contribution to achieving the UNAIDS 90-90-90 target. However, this will only be possible with progress in the first stage in the HIV care cascade, the 90% diagnosis target, as even a small number of undiagnosed people could sustain an epidemic [58]. Also, other stages of the HIV care continuum not directly measured in the 90-90-90 scheme are important to reach the UNAIDS target, such as linking diagnosed HIV-positive patients to services and ensuring sustained and appropriate care, like switching to second-line therapy regimens when necessary [27]. Indeed, we found increased access to ART and viral suppression in stronger health systems, which are likely to provide better retention within the system because of increased availability, accessibility and affordability of services. Thus, achieving the 90-90-90 target will require both HIV-specific measures, such as test-and-treat policies and universal access to ART, and also general improvements to the health system.

There are some limitations to this study. The first is the risk of ecological fallacy. While exposure to a given ART initiation guideline is a national policy that should apply to everyone, we cannot exclude the possibility that some populations subject to stigma and discrimination might be treated differently. For instance, only about half of the countries in Europe and Central Asia offer HIV treatment to undocumented migrants [59]. Other populations that are also likely to suffer differential provision of HIV health care services are sex workers [60,61] and people who inject drugs [62,63]. Consequently, our results are likely to be conservative estimates of the association between ART initiation policies and population-level access to ART. A second, linked, limitation is the assumption that adoption of the guidelines translated into implementation. If failure to implement guideline recommendations was randomly distributed across various ART initiation policies, this would have yielded conservative estimates. Nonrandom variation would have yielded biased estimates. However, many countries adopted the guidelines some time before the reporting date and can be expected to have rolled them out to ART services. Thirdly, there could be measurement error in the outcome variables as a result of different data collection procedures and misclassification of outcome status, which could have biased our estimates, diluting findings and making it harder to ascertain an association. Indeed, some countries reported very low levels of viral suppression; however, it is possible that these measurements were affected by different factors, including treatment disruptions (voluntary or as a result of stock-outs), use of first or second line of treatment, loss to follow-up, transfer of care (people moving to another clinic may show up as having been lost to follow-up), out-migration, poor monitoring systems (tracking people and collecting data), and infrequent viral load measurements. A fourth limitation is the small sample size used in the study, potentially generating imprecise estimates of associations. However, the finding of similar results in the larger sample, notwithstanding the greater data problems, offers reassurance. A fifth limitation is that, of the 48 countries that responded to the survey, 37 countries had data available on ART coverage and 30 had data on viral suppression of all people living with HIV [41,42]. Those that either failed to respond or lacked data were mainly from non-EU/EEA, Eastern European and Central Asian countries that might have different characteristics from the countries included in the analyses, which could have biased our estimates. Sixthly, we used cross-sectional data measuring exposure and outcome simultaneously. Reverse causality is a risk but is unlikely because, while it is theoretically possible that a greater proportion of people on ART and virally suppressed could have exerted pressure for expanded ART initiation policies, the association is much more likely to flow from expanded ART initiation policies to a greater percentage of people on ART and virally suppressed. Another limitation of cross-sectional data is that they do not capture any lag effect between policy adoption and treatment initiation. If there were lagged effects, our estimates could be biased towards the null. Finally, the country data used were drawn from different years, reflecting the limitations of the country surveillance and reporting systems; however, this did not affect our ability to test our question across countries and years, and as a robustness check the models were adjusted for the year of data availability to account for the potential effect of secular trends.

To our knowledge, this is the first ecological cross-national analysis evaluating the impact of test-and-treat on achievement of the 90-90-90 target internationally, adjusting for several possible confounders. We offer evidence of an association between test-and-treat guidelines and greater treatment coverage and viral suppression rates at the population level among people with diagnosed HIV infection and on ART, respectively. While it cannot be regarded as conclusive, it provides evidence that must be assessed further using other research designs, which could, for instance, include longitudinal data for all countries. The cross-national character of this study, including a broad variety of countries from Europe and Central Asia, gives external validity to the findings and the potential to generalize to other contexts.

Our results have important policy implications. First, they support the recommendation of test-and-treat policies by the WHO and EACS as a means to achieve the UNAIDS 90-90-90 target for 2020, which also align with the Sustainable Development Goal target to end the HIV epidemic by 2030. Secondly, they show that test-and-treat policies can achieve results comparable to those that might otherwise be expected with very large investments in public health services. Thirdly, they reinforce the case for intensification of efforts to expand new test-and-treat policies in Eastern European and Central Asian countries. However, our results do not provide guidance on how to implement test-and-treat. A next step in research would be to test empirically how to operationalize its implementation, along with the necessary services. Taken together, our results are consistent with a growing body of research indicating that test-and-treat is an effective means to reducing the burden of disease attributable to HIV.

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Conflicts of interest: None of the authors has competing interests to declare.

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Author contributions

JCS initiated the study. AML and DS designed the study. AML collected the data, implemented the study, and wrote the first draft of the manuscript. MM, DS, RG, SG, TN and JCS offered comments on the draft and helped interpret the findings.

References

1 World Health Organization. Treat all people living with HIV, offer antiretrovirals as additional prevention choice for people at “substantial” risk. 2015.

2 World Health Organization. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. 2015.

3 European AIDS Clinical Society. Guidelines. Version 8.0. October 2015. 2015.

4 Guay LA, Musoke P, Fleming T *et al.* Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet* 1999; **354**: 795–802.

5 Siegfried N, van der Merwe L, Brocklehurst P, Sint TT. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database Syst Rev* 2011: Cd003510.

6 Musicco M, Lazzarin A, Nicolosi A *et al.* Antiretroviral treatment of men infected with human immunodeficiency virus type 1 reduces the incidence of heterosexual transmission. Italian Study Group on HIV Heterosexual Transmission. *Arch Intern Med* 1994; **154**: 1971–1976.

7 Quinn TC, Wawer MJ, Sewankambo N *et al.* Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* 2000; **342**: 921–929.

8 Taylor S, Boffito M, Vernazza PL. Antiretroviral therapy to reduce the sexual transmission of HIV. *J HIV Ther* 2003; **8**: 55–66.

9 Montaner JSG, Hogg R, Wood E *et al.* The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 2006; **368**: 531–536.

10 AG ESÄ. HIV-infizierte Menschen ohne andere STD sind unter wirksamer antiretroviraler Therapie sexuell nicht infektiös. 2008.

11 Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009; **23**: 1397–1404.

12 Cohen MS, Chen YQ, McCauley M *et al.* Prevention of HIV-1 Infection with Early Antiretroviral Therapy. *N Engl J Med* 2011; **365**: 493–505.

13 Anglemyer A, Rutherford GW, Horvath T, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database Syst Rev* 2013: Cd009153.

14 Loutfy MR, Wu W, Letchumanan M *et al.* Systematic review of HIV transmission between heterosexual serodiscordant couples where the HIV-positive partner is fully suppressed on antiretroviral therapy. *PLoS ONE* 2013; **8**: e55747.

15 Rodger A, Bruun T, Cambiano V, Vernazza P, Strada V, Van Lunzen J, eds. 153LB: HIV transmission risk through condomless sex if HIV+ partner on suppressive ART: PARTNER Study. *21st Conference on Retroviruses and Oppotunistic Infections*; 2014.

16 Cohen MS, Chen YQ, McCauley M *et al.* Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med* 2016; **375**: 830–839.

17 Smith MK, Powers KA, Muessig KE, Miller WC, Cohen MS. HIV treatment as prevention: the utility and limitations of ecological observation. *PLoS Med* 2012; **9**: e1001260.

18 Katz MH, Schwarcz SK, Kellogg TA *et al.* Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health* 2002; **92**: 388–394.

19 Eaton LA, Kalichman S. Risk compensation in HIV prevention: implications for vaccines, microbicides, and other biomedical HIV prevention technologies. *Curr HIV/AIDS Rep* 2007; **4**: 165–172.

20 Cassell MM, Halperin DT, Shelton JD, Stanton D. Risk compensation: the Achilles’ heel of innovations in HIV prevention? *BMJ* 2006; **332**: 605–607.

21 Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. *JAMA* 2004; **292**: 224–236.

22 Kennedy C, O’Reilly K, Medley A, Sweat M. The impact of HIV treatment on risk behaviour in developing countries: a systematic review. *AIDS Care* 2007; **19**: 707–720.

23 Suzan-Monti M, Lorente N, Demoulin B *et al.* Sexual risk behaviour among people living with HIV according to the biomedical risk of transmission: results from the ANRS-VESPA2 survey. *J Int AIDS Soc* 2016; **19**: 20095.

24 Venkatesh KK, Flanigan TP, Mayer KH. Is expanded HIV treatment preventing new infections? Impact of antiretroviral therapy on sexual risk behaviors in the developing world. *AIDS* 2011; **25**: 1939–1949.

25 Vella S. Addressing barriers to the end of AIDS by 2030. *Lancet HIV* 2015; **2**: e360–e361.

26 Kulkarni SP, Shah KR, Sarma KV, Mahajan AP. Clinical uncertainties, health service challenges, and ethical complexities of HIV “test-and-treat”: a systematic review. *Am J Public Health* 2013; **103**: e14–e23.

27 Bain LE, Nkoke C, Noubiap JJN. UNAIDS 90–90–90 targets to end the AIDS epidemic by 2020 are not realistic: comment on “Can the UNAIDS 90–90–90 target be achieved? A systematic analysis of national HIV treatment cascades”. *BMJ Glob Health* 2017; **2**: e000227.

28 The Lancet HIV: the question is not when to treat, but how to treat. *Lancet* 2015; **386**: 1420.

29 Shelton JD, Cohen M, Barnhart M, Hallett T. Is antiretroviral therapy modifying the HIV epidemic? *Lancet* 2010; **376**: 1824–1825; author reply 5.

30 Wilson DP. HIV treatment as prevention: natural experiments highlight limits of antiretroviral treatment as HIV prevention. *PLoS Med* 2012; **9**: e1001231.

31 Nansseu JRN, Bigna JJR. Antiretroviral therapy related adverse effects: can sub-Saharan Africa cope with the new "test and treat" policy of the World Health Organization? *Infect Dis Poverty* 2017; **6**: 24.

32 Montaner JS. Treatment as prevention: toward an AIDS-free generation. *Top Antivir Med* 2013; **21**: 110–114.

33 Montaner JS, Lima VD, Barrios R *et al*. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet* 2010; **376**: 532–539.

34 Montaner JS, Lima VD, Harrigan PR *et al*. Expansion of HAART coverage is associated with sustained decreases in HIV/AIDS morbidity, mortality and HIV transmission: the "HIV Treatment as Prevention" experience in a Canadian setting. *PLoS ONE* 2014; **9**: e87872.

35 Das M, Chu PL, Santos GM *et al*. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS ONE* 2010; **5**: e11068.

36 Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science* 2013; **339**: 966–971.

37 Fang CT, Hsu HM, Twu SJ *et al*. Decreased HIV transmission after a policy of providing free access to highly active antiretroviral therapy in Taiwan. *J Infect Dis* 2004; **190**: 879–885.

38 Granich R, Gupta S, Hersh B *et al*. Trends in AIDS deaths, new infections and ART coverage in the top 30 countries with the highest AIDS mortality burden; 1990-2013. *PLoS ONE* 2015; **10**: e0131353.

39 European Centre for Disease Prevention and Control (ECDC). Special report: continuum of HIV care. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report. Stockholm: European Centre for Disease Prevention and Control; 2017.

40 European Centre for Disease Prevention and Control (ECDC). Special report: HIV treatment and care. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report. Stockholm: European Centre for Disease Prevention and Control; 2017.

41 Gourlay AJ, Pharris AM, Noori T *et al*. Towards standardised definitions for monitoring the continuum of HIV care in Europe. *AIDS* 2017; **31**: 2053–2058.

42 Drew RS, Rice B, Rüütel K *et al*. HIV continuum of care in Europe and Central Asia. *HIV Med* 2017; **18**: 490–499.

43 Raymond A, Hill A, Pozniak A. Large disparities in HIV treatment cascades between eight European and high-income countries - analysis of break points. *J Int AIDS Soc* 2014; **17** (4 Suppl 3): 19507.

44 European Centre for Disease Control (ECDC), World Health Organization (WHO) Regional Office for Europe. HIV/AIDS surveillance in Europe 2018 – 2017 data. Copenhagen; 2018.

45 European Centre for Disease Prevention and Control (ECDC). Special report: the status of the HIV response in the European Union/European Economic Area, 2016. Stockholm: European Centre for Disease Prevention and Control; 2017.

46 (ECDC) ECfDC. Joint technical mission: HIV in Greece 28–29 May 2012. ECDC. 2013.

47 Global HIV Policy Watch [Internet]. April 2017. Available at http://www.hivpolicywatch.org/ (accessed 15 January 2018).

48 Global 90-90-90 Watch [Internet]. April 2017. Available at http://hiv90-90-90watch.org/ (accessed 15 January 2018).

49 World Bank Open Data [Internet]. 2016. Available at http://data.worldbank.org/ (accessed 15 July 2017).

50 Castel AD, Befus M, Willis S *et al*. Use of the community viral load as a population-based biomarker of HIV burden. *AIDS* 2012; **26**: 345–353.

51 Dutta A, Barker C, Kallarakal A. The HIV treatment gap: estimates of the financial resources needed versus available for scale-up of antiretroviral therapy in 97 countries from 2015 to 2020. *PLoS Med* 2015; **12**: e1001907.

52 Tao LL, Liu M, Li SM *et al*. Impact of antiretroviral therapy on the spread of human immunodeficiency virus in Chaoyang District, Beijing, China: using the Asian Epidemic Model. *Chin Med J* 2017; **130**: 32–38.

53 Caro-Vega Y, del Rio C, Lima VD *et al*. Estimating the impact of earlier ART initiation and increased testing coverage on HIV transmission among men who have sex with men in Mexico using a mathematical model. *PLoS ONE* 2015; **10**: e0136534.

54 Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009; **373**: 48–57.

55 Lima VD, Johnston K, Hogg RS *et al*. Expanded access to highly active antiretroviral therapy: a potentially powerful strategy to curb the growth of the HIV epidemic. *J Infect Dis* 2008; **198**: 59–67.

56 Althoff KN, Buchacz K, Hall HI *et al*. U.S. trends in antiretroviral therapy use, HIV RNA plasma viral loads, and

CD4 T-lymphocyte cell counts among HIV-infected persons, 2000 to 2008. *Ann Intern Med* 2012; **157**: 325–335.

57 Sorensen SW, Sansom SL, Brooks JT *et al.* A mathematical model of comprehensive test-and-treat services and HIV incidence among men who have sex with men in the United States. *PLoS ONE* 2012; **7**: e29098.

58 Hill A, Pozniak A. HIV treatment cascades: how can all countries reach the UNAIDS 90–90–90 target? *AIDS* 2015; **29**: 2523–2525.

59 European Centre for Disease Prevention and Control (ECDC). Special report: HIV and migrants. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report. Stockholm: European Centre for Disease Prevention and Control; 2017.

60 Reeves A, Steele S, Stuckler D, McKee M, Amato-Gauci A, Semenza JC. National sex work policy and HIV prevalence among sex workers: an ecological regression analysis of 27 European countries. *Lancet HIV* 2017; **4**: e134–e140.

61 Reeves A, Steele S, Stuckler D, McKee M, Amato-Gauci A, Semenza JC. Gender violence, poverty and HIV infection risk among persons engaged in the sex industry: cross-national analysis of the political economy of sex markets in 30 European and Central Asian countries. *HIV Med* 2017; **18**: 748–755.

62 European Centre for Disease Prevention and Control (ECDC). Evidence brief: impact of stigma and discrimination on access to HIV services in Europe. Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia. Stockholm: European Centre for Disease Prevention and Control; 2017.

63 European Centre for Disease Prevention and Control (ECDC). Evidence brief: HIV and laws and policies in Europe. Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia. Stockholm: European Centre for Disease Prevention and Control; 2017.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Latest antiretroviral therapy initiation guidelines by country and year of adoption for countries with test-and-treat (as of August 2017).
Table S2. List of countries, region, year of data availability, and antiretroviral therapy policy in the year of data availability.
Table S3. Summary of ECDC data sources for 90-90-90: access to ART and viral suppression.
Table S4. Descriptive statistics for countries.

2.5 Study 5: The mental health crisis during the COVID-19 pandemic in older adults and the role of physical distancing interventions and social protection measures in 26 European countries

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The mental health crisis during the COVID-19 pandemic in older adults and the role of physical distancing interventions and social protection measures in 26 European countries

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ABSTRACT

Background: The COVID-19 pandemic and associated policy responses, such as physical distancing interventions, pose risks to mental health that could be mitigated by social support systems. We examine associations between changes in mental health in the population aged 50 years and older in Europe and stringency of pandemic responses and social protection.

Methods: We analysed data from the Survey of Health, Ageing and Retirement in Europe: n = 50,278 individuals aged 50 years and older in 26 European countries between June and August 2020. Linear multivariable regression models were used to evaluate potential risk factors for deterioration in self-reported mental health and investigate whether social protection systems mitigate it.

Results: Across the European Union, 28.1% (95% CI:27.1–29.2) of participants reported worsening mental health since the beginning of the pandemic, ranging from 16.1% in Slovakia to 54.8% in Portugal. Factors associated with increased risk of deterioration included: being female (12.7 percentage points (ppt), 95%CI:9.2–16.2); experiencing unmet healthcare needs during the pandemic (14.6 ppt, 95%CI:11.2–18.1); job loss during the pandemic (6.2 ppt, 95%CI:1.1–11.8); and financial hardship (5.1 ppt, 95%CI:2.9–7.2). Greater stringency of physical distancing measures in countries was associated with worsening mental health (0.2 ppt per each one point increase on a stringency index, 95% CI:0.09–0.4); however, country-level pre-pandemic expenditures on various social protection packages was associated with decreased probability of worsening mental health (−1.3 ppt, 95%CI: 0.3 to −2.3 per €1,000 increase in health care expenditures per capita and, among the unemployed, −3.8 ppt, 95%CI: 1.6 to −2.4 per €100 increase in unemployment expenditure per capita).

Conclusions: The COVID-19 pandemic has been associated with substantial mental health deterioration exhibiting social inequalities. Adverse mental health has been exacerbated by policy responses to the pandemic regulating physical distancing, but social protection expenditure might have helped mitigate the impact. Strengthening social protection systems might render the mental health of the population more resilient to the consequences of crises such as the COVID-19 pandemic.

1. Introduction

The COVID-19 pandemic and corresponding responses have massively disrupted daily life in many countries, with profound consequences for mental health and wellbeing, especially those whose lives were already precarious. In response, the United Nations has called for mental health protection to be made a policy priority (United Nations Secretary-General Policy Brief, 2020). Mental health is threatened by multiple pandemic-related stressors, including insecurity of income and employment, isolation, and loss of social support, inability to access

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essential services such as health and education, and fear of contracting COVID-19 and becoming severely ill or dying.

A review of the evidence on the psychological impact of quarantine found that most studies reported negative psychological effects (Brooks et al., 2020), and systematic reviews on the specific impact of the COVID-19 pandemic on mental health found a deterioration of mental health in the general population, but with significant differences among socioeconomic groups (Vindegaard & Benros, 2020; Wang et al., 2020; Xiong et al., 2020). Several more recent studies have also found similar findings (Ettman et al., 2020; Fancourt et al., 2021; González-Sanguino et al., 2020; Pan et al., 2021; M. Pierce, Hope, et al., 2020). Although some of these studies have used data representative of populations, many use non-representative samples, such as those recruited using the internet, which can introduce bias as those who experience digital exclusion, including many older or poorer people or those with mental illness, and who are at increased risk from both COVID-19 and policy responses, may be excluded (Sounderajah et al., 2021). As a consequence, there have been calls for greater use of high-quality representative data that can provide more robust evidence on the impact of the pandemic on mental health (Holmes et al., 2020; Matthias Pierce, McManus, et al., 2020b).

Underrepresentation of older people is especially problematic. The World Health Organization has viewed the mental health of older adults as a particular concern in the COVID-19 pandemic, especially those who are isolated or experience cognitive decline (World Health Organization, 2020c), as older population have been at highest risk of complications and death from COVID-19 (Lloyd-Sherlock et al., 2020). On the other hand, there is some evidence that older adults may be more resilient, at least in the short-term, to some of the harms arising from the COVID-19 pandemic (Vahia et al., 2020). However, depression outcomes among older populations are, as in all population groups, characterized by sociodemographic inequalities (Richardson et al., 2020). Additionally, the pattern of sociodemographic inequalities varies substantially across countries (Richardson et al., 2020). The apparent mental health resilience of older adults to the effects of the COVID-19 pandemic may also vary across countries, as will the exposure of older adults to risk and protective factors (World Health Organization, 2020a), plausibly because of differences in policy responses that offer protection.

Countries have adopted different responses to control of the pandemic. They entered it with different social support systems, with implications for their resilience to adversity, shocks, and crises. Social protection policies can provide a safety net to protect against the negative consequences of adverse life events and conditions, while promoting social and health equity. A study from the United States found that people living in states with more supportive social policies experienced less impact on mental health when exposed to COVID-19-related household income shocks (Donnelly & Farina, 2021). Given the often more generous welfare regimes in European countries, we might expect to see at least the same effect, but the greater diversity in Europe may offer additional insights. Thus, different social protection systems might be expected to offer differing levels of protection.

Here we seek a broad understanding of how older people in Europe have experienced the effects of the pandemic on mental health, looking first at socioeconomic inequalities and stressors placed upon the population, such as income and employment insecurity and potential isolation resulting from physical and social distancing measures. Second, measures that might mitigate these effects, in the form of existing social protection measures. We thus use harmonised cross-national, nationally representative survey data to provide estimates of the prevalence of self-reported decline in mental health during the COVID-19 pandemic. We describe differences within the population aged 50 years or older and among 26 European countries, with a focus on socioeconomic characteristics of participants before and during the pandemic, assessing whether the stringency of policy responses to the pandemic in Europe, in terms of containment and closure measures, affected the mental health of older populations. Finally, we test whether and to what extent social protection expenditures influence their mental health.

2. Methods

2.1. Sources of data

We used data from the Survey of Health, Ageing and Retirement in Europe (SHARE) COVID-19 survey. Details of the dataset have been describe elsewhere (Börsch-Supan et al., 2013). Briefly, SHARE COVID-19 is a cross-sectional dataset with information on health, social and environmental characteristics of adults aged 50 years or older in 27 European countries and Israel, with samples that are nationally representative. The SHARE COVID-19 data were collected via computer-assisted telephone interviews between June and August 2020 using a survey harmonised ex-ante and translated into the national languages (Börsch-Supan, 2020).

The SHARE COVID-19 cross-sectional dataset contains data on 50,278 individuals (representing, when weighted, a population of 180,358,661 individuals) aged 50 years or older who reported whether their mental health status had worsened from before the pandemic. Information on survey non-response is currently not available. Respondents are from the 26 European countries for which there are publicly available data (25 European Union countries (which excludes Austria and Ireland because data were not available) and Switzerland. The countries included are Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Lithuania, Luxembourg, Latvia, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and Switzerland. Israel was not included in this study.

SHARE is a multinational survey using probability-based sampling. Because data are collected by national agencies, differences in sampling methods and resources between countries exist, particularly in access to official person registries covering the population of interest including information on age. SHARE sampling details for each country can be found elsewhere (Bergmann et al., 2019; Börsch-Supan, 2020; Börsch-Supan et al., 2013). All respondents provided informed consent.

Data on social protection system expenditures were taken from Eurostat for the latest available year (2018) (Eurostat, 2021). Data on country-level COVID-19 incidence as of 1st June of 2020 and data on the stringency of government policy measures were taken from Our World in Data database, which are sourced, respectively, from Johns Hopkins University (Dong et al., 2020) and the Oxford Coronavirus Government Response Tracker (OxCGRT) (Hale et al., 2021).

2.2. Outcome measure

Worsened mental health was measured as self-reported decline in mental health between the inception of the pandemic and the month prior to responding to the survey. Specifically, it combined data collected in response to four questions asking: “In the last month, have you been sad or depressed?” and “In the last month, have you felt nervous, anxious or on edge?“, both questions followed by “Has that been more so, less so, or about the same as before the outbreak of Corona?“. For the first two questions, the possible answers were either positive or negative. Those who responded affirmatively were asked the last question, with possible answers “More so”, “Less so” or “About the same”. We classified individuals who responded “More so” to either the question referring to sadness and/or depression or the question about having felt nervous, anxious, and/or on edge as having experienced worsened mental health during the outbreak; all other responses were classified as not having experienced worsened mental health.

2.3. Individual-level socio-economic and health measures

To capture the socioeconomic impact of the pandemic on mental health, we included a series of variables on demographic and socioeconomic characteristics before and during the pandemic that measured income insecurity, unemployment, and socialization. We also capture the impact of health-related variables during the pandemic on worsened mental health, including the impact of personally experiencing COVID-19 or having someone close experience it, as well as the effect of foregone healthcare. Fig. 1 illustrates the pathways of pandemic-related stressors on mental health deterioration.

The included variables are *age*, an ordinal variable categorized in the following three groups: 50–64 years old, 65–79 years old, and 80 years old and older; *gender*, a dichotomous variable with the categories male and female; *self-rated health before the pandemic* is an ordinal variable measuring the self-reported health status of the respondent before the pandemic including the categories excellent, very good, good, fair, and poor; *COVID-19 positive* is a dichotomous variables measuring whether the responded had tested positive for the virus; *anyone known with a COVID-19 positive test* is a dichotomous variable measuring whether someone close to the respondent tested positive for the virus; *foregone healthcare during the pandemic* is a dichotomous variables that measures whether the respondent had impeded healthcare service access during the pandemic; *household size* is a dichotomous variable measuring whether the respondent lives alone or in a household of two people or more; *working before the pandemic* is a dichotomous variable capturing whether the respondent was working before the pandemic or was unemployed or retired; *became unemployed during the pandemic* is a dichotomous variable measuring whether among those working, the respondent became unemployed during the pandemic; and *make ends meet* is an ordinal variable measuring the ability of the household to live on their available economic resources during the pandemic and includes the categories with great difficulty, with some difficulty, fairly easily, and easily.

2.4. Lockdown measures

The severity of lockdown measures was captured using the Oxford Stringency Index of government policy responses to the coronavirus pandemic. Details on how OxCGRT constructs the Stringency Index are available elsewhere (Hale et al., 2021). Briefly, the Stringency Index aggregates various measures of governments' responses to the pandemic capturing variations across countries in measures to increase physical distancing, such as school and work closures, stay-at-home orders, cancelling public events and restrictions on gathering sizes, public transport closures, and restrictions on internal and international travel. The Stringency Index measures policy responses per day since the January 1, 2020, taking a value between 1 and 100, where a higher score indicates a stricter government response. To capture the stringency of lockdown measures over time, we used the average of the daily values for the period between the day after the declaration of the outbreak as public health emergency of international concern by the World Health Organization (January 31, 2020) (World Health Organization, 2020b) and the initiation of the SHARE COVID-19 fieldwork (June 1, 2020) (Börsch-Supan, 2020). Fig. 2 illustrates the pathways of impact of lockdown measures directly on mental health deterioration (see pandemic-related stressor in Fig. 1) and through the economic shock associated to physical distancing measures.

2.5. Social protection measures

To assess the role of each country's social protection system on the change in mental health during the pandemic, we incorporated a series of ecologic variables measuring national expenditure on social protection systems pre-pandemic, using data for 2018, the latest available year. These variables included spending on a full package of social protection benefits as well as on the categories of healthcare/sickness, old-age/pensions, and unemployment. The full package of social protection benefits comprises expenditures on disability, sickness/healthcare, old age, survivors, family/children, unemployment, housing, and social exclusion not covered elsewhere. Healthcare expenditures include current expenditures on healthcare goods and services. Pension expenditures include disability pension, early retirement due to reduced capacity to work, old-age pension, anticipated old-age pension, partial pension, survivors' pension, and early retirement due to labour market factors. Unemployment expenditures include spending on benefits for unemployed persons such as cash benefits, vocational training allowances, redundancy compensations, placement services and job search assistance. Data are measured as expenditures per inhabitant in Euros adjusted for purchasing power parities. Fig. 2 illustrates the pathway by which social protection expenditures might impact mental health, where social protection moderates the economic shock resulting from the pandemic-related physical distancing measures.

2.6. Statistical analyses

First, we report estimates of the prevalence of worsened mental health overall and disaggregated by mental health condition: depression and/or sadness, and feeling anxious, nervous, and/or on edge. We estimated prevalence as the proportion of individuals reporting having

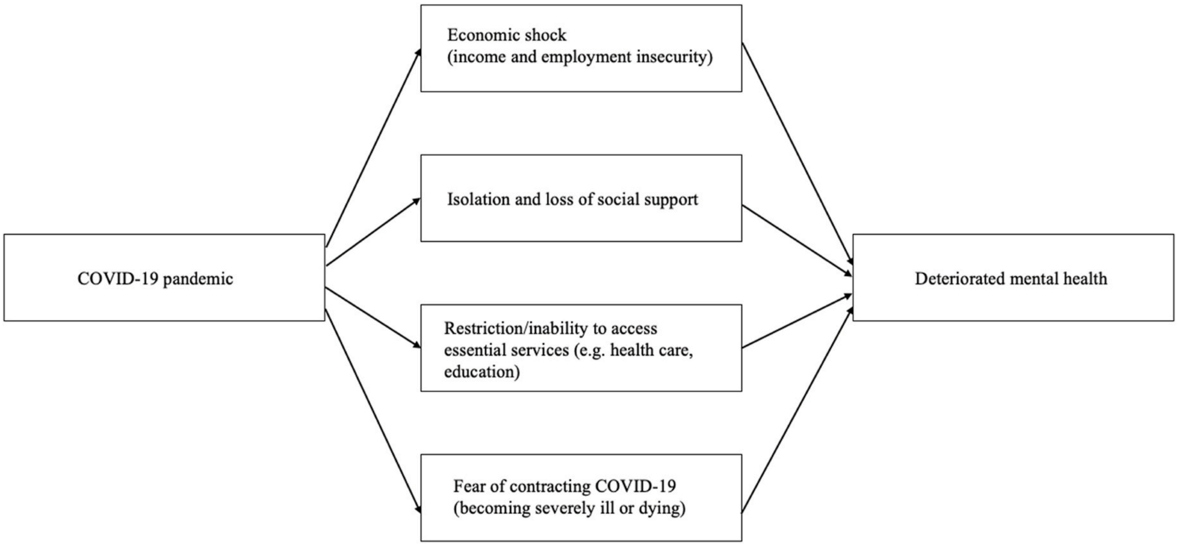

Fig. 1. DAG of the pathways of pandemic-related stressors on mental health deterioration.

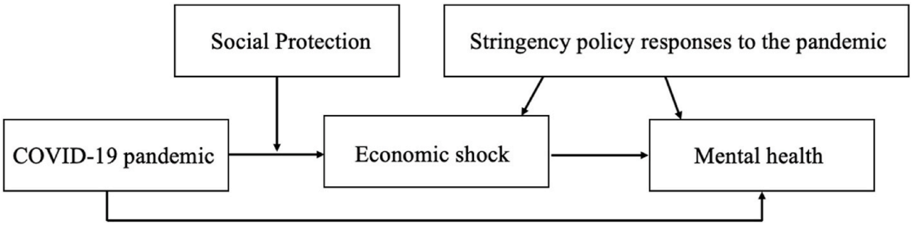

Fig. 2. DAG of the pathways of country-level determinants of mental health deterioration.

experienced an adverse mental health outcome. We also report the prevalence of worsened mental health by age, sex, COVID-19 infection status, ability of the individual's household to make ends meet, and by country. Chi-square tests for proportions and linear trend were performed to explore unadjusted statistical differences between groups. We used calibrated individual weights to adjust the prevalence estimates for the different selection probabilities and non-response rates.

Second, country fixed-effects multivariable linear probability models were used to evaluate individual-level determinants of change in the probability of worsened mental health (equation (1)), as follows:

$$\text{Worsened mental health}_{i,c} = \alpha + \beta + \beta\text{SocDem}_{i,c} + \beta\text{Health}_{i,c} + \beta\text{COVID-19 positive}_{i,c} + \beta\text{Foregone care}_{i,c} + \beta\text{Household size}_{i,c} + \beta\text{Make ends meet}_{i,c} + \beta\text{Employment}_{i,c} + \mu_c + \varepsilon_{i,c} \quad (1)$$

where *i* is individual and *c* is country. *Worsened mental health* measures self-reported worsened mental health since the beginning of the pandemic. *SocDem* is a vector of sociodemographic variables, including age and gender. *Health* measures self-rated health before the pandemic and serves as an adjustment to limit the effect of confounding due to previous poor health. *COVID-19 positive* is a vector of two variables indicating whether the respondent tested positive for COVID-19 or someone close to them did. *Employment* is a vector of two variables measuring, first, whether the respondent was working before the pandemic, and, second, whether among those working, the respondent became unemployed during the pandemic. The other terms in the equation correspond to the definitions provided above. μ was used to capture unobserved country characteristics; ε is the error term. We report robust standard errors clustered by country to account for within country correlation and used calibrated individual weights.

Next, we used multivariable linear probability models to evaluate country-level determinants of worsened mental health. First, we test whether, in countries with a greater toll of the pandemic on population health measured as total cases per million inhabitant, mental health had further deteriorated. Second, we test whether in countries with more stringent lockdown response measures to the pandemic, individuals had worsened metal health. We evaluate this association with the overall stringency index as well as each of its components. Third, we test whether more generous social protection systems, measured as higher

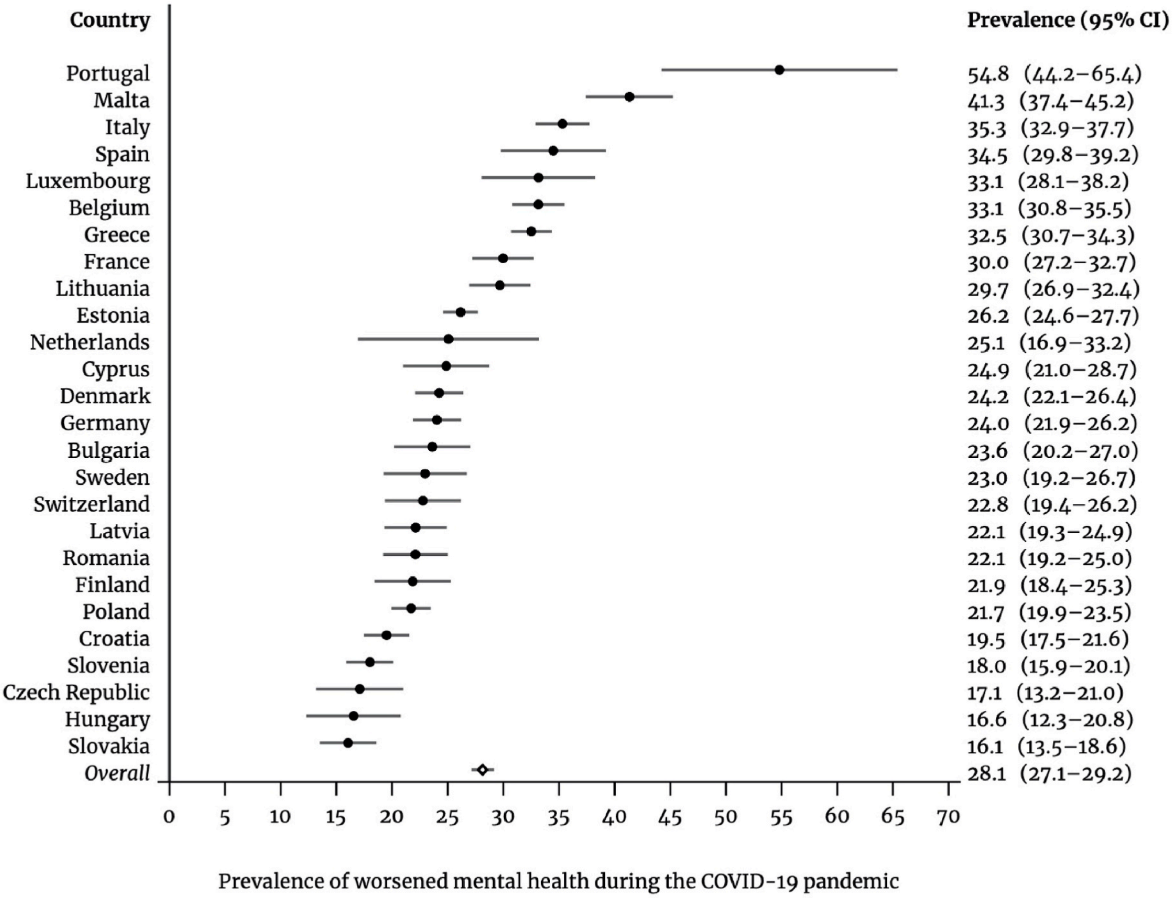

Fig. 3. Prevalence of worsened mental health due to the COVID-19 pandemic in 26 European countries, June–August 2020.

social protection expenditures, may mitigate mental health deterioration, for which we perform analyses for the overall sample or affected population subgroups. Calibrated individual weights were used in all models. Missing data were handled with pairwise deletion. Analyses were performed using Stata 16.1 (StataCorp, 2019).

3. Results

3.1. Prevalence of worsened mental health during the COVID-19 pandemic

Across all countries, the prevalence of worsened mental health during the COVID-19 pandemic, compared to before, was 28.1% (95% CI: 27.1–29.2), ranging from 16.1% in Slovakia to 54.8% in Portugal (Fig. 3). Looking at each mental health condition, 18.1% of the respondents reported experiencing worsened depression and/or sadness, 22.1% worsened feelings of being anxious, nervous and/or on edge, and 12.0% reported experiencing both (Table 1).

The prevalence was higher for women, of whom 34.4% (95% CI: 33.1–35.7) reported worsened mental health during the pandemic, which is 13.7 percentage points (ppt) above the 20.7% (95% CI: 19.2–22.3) prevalence among men (Table 2). People aged 80 years or older reported slightly worsened mental health (30.6%, 95% CI: 29.0–32.2) compared to the age group 65–79 years old (27.1%, 95% CI: 26.1–27.9) but no different from the age group 50–64 years old (28.1%, 95% CI: 26.2–30.1). There was no trend in the reported prevalence estimates across age groups (p-value = 0.261). Individuals who had been infected with COVID-19 had a prevalence of worsened mental health of 41.7% (95% CI: 29.2–54.2), which was 13.7 ppt above the prevalence among those who had not contracted the virus (28.0%, 95% CI: 27.0–29.1). The prevalence of worsened mental health was also higher for people who had someone close to them who had been infected (33.5%, 95% CI: 28.7–38.4, vs. 27.6, 95% CI: 26.6–28.6). Looking at economic status, individuals with greater capacity to make ends meet were less likely to report worsened mental health (p-value <0.0001). Individuals who faced great difficulty making ends meet reported a 13.9 ppt higher prevalence than individuals who easily made ends meet (25.0%, 95% CI: 23.2–26.9 and 38.9%, 95% CI: 35.6–42.4, respectively). The prevalence of worsened mental health for those facing some difficulty making ends meet was 31.9% (95% CI: 29.6–34.1) and in those finding it fairly easy to make ends meet was 26.2% (95% CI: 24.5–27.8).

Thus, we found that the greatest prevalence of worsened mental health occurred among individuals who had tested positive for COVID-19 (41.7%, 95% CI: 29.2–54.2), those with great difficulty to make ends meet (38.9%, 95% CI: 35.6–42.4), women (34.4%, 95% CI: 33.1–35.7), individuals who had someone close to them test positive for COVID-19 (33.5%, 95% CI: 28.7–38.4), individuals with some difficulty to make ends meet (31.9%, 95% CI: 29.6–34.1), and individuals aged 80 years old and older vs those aged 65–79 years old (30.6%, 95% CI: 29.0–32.2).

3.2. Risk factors for worsening mental health during the COVID-19 pandemic

Table 3 shows estimates of the change in the probability of reporting worsened mental health during the COVID-19 pandemic according to multiple individual-level determinants. Estimates from the fully adjusted regression model show that women had a 12.7 ppt higher probability than men of reporting worsened mental health (95% CI: 9.2–16.2). The probability of reporting worsened mental health was lower for individuals aged 80+, compared with those aged 50–65 (80+ vs 50–64 years old: 4.1 ppt, 95% CI: 0.7 to −7.5; 65–79 years old vs 50–64: 2.9 ppt, 95% CI: 7.2–1.4).

Turning to direct experience of COVID-19, those who had tested positive were 12.5 ppt (95% CI: 0.7–24.3) more likely to report worsened mental health than those who had not but having someone close test positive had no effect (2.9 ppt, 95% CI: 1.9–7.7). Self-rated health before the pandemic showed a dose-response relationship with worsened mental health. Those whose general health had been worse were more likely to report worsening mental health (poor vs excellent health: 21.3 ppt, 95% CI: 17.6–25.0; fair vs excellent health: 14.6 ppt, 95% CI: 11.2–18.1; good vs excellent health: 5.8 ppt, 95% CI: 2.2–9.4; and very good vs excellent health: 1.3 ppt, 95% CI: 1.9–4.5). Individuals foregoing healthcare had a higher probability of reporting worsened mental health, by 14.2 ppt (95% CI: 12.0–16.5).

Table 1
Descriptive statistics of study population, June–August 2020.

	N	Unweighted proportion or mean (SD)	Weighted proportion or mean (SD)
Total sample	50,278	100.0	100.0
Total population	180,358,661	100.0	100.0
Sociodemographic variables			
Age groups; 50–64	14,793	29.23	48.43
65-79	26,550	52.46	35.58
80+	9,266	18.31	15.99
Gender; Female	29,422	57.86	54.03
Health-related variables			
Worsened mental health; Yes	13,504	26.69	28.14
Worsened depression; Yes	8,299	16.41	18.05
Worsened anxiety; Yes	10,820	21.39	22.13
Worsened depression and anxiety; Yes	5,615	11.04	11.97
Self-rated health before pandemic; Excellent	3,377	6.68	7.18
Very good	7,986	15.79	17.83
Good	22,455	44.39	47.01
Fair	13,155	26.01	22.06
Poor	3,608	7.13	5.93
COVID-19 positive test; Yes	238	0.47	0.77
Anyone known COVID-19 positive test; Yes	3,363	6.69	8.86
Forgone healthcare during pandemic; Yes	5,991	11.85	11.57
Socioeconomic variables			
Living alone; Yes	12,301	24.19	27.07
Working before pandemic; Yes	10,744	21.25	32.88
Became unemployed during pandemic; Yes	1,949	3.85	6.67
Make ends meet during pandemic; With great difficulty	4,683	9.51	8.49
With some difficulty	12,993	26.38	23.79
Fairly easily	17,233	34.99	36.18
Easily	14,346	29.13	31.55
Country-level variables			
Total COVID-19 cases per million inhabitants	26 countries	2,090.89 (1,690.31)	2,640.67 (1,468.72)
Stringency index of policy responses to the pandemic	26 countries	56.41 (7.39)	61.15 (5.43)
Social protection expenditures per capita in Euros, PPS	26 countries	6,972.92 (3,001.77)	8,161.31 (2,760.94)
Healthcare expenditures per capita in Euros, PPS	26 countries	1,936.97 (908.18)	2,385.93 (1,072.76)
Unemployment expenditures per capita in Euros, PPS	26 countries	291.17 (208.32)	359.77 (187.26)
Old age expenditures per capita in Euros, PPS	26 countries	2,935.51 (1,116.10)	3,312.86 (923.18)

SD: Standard deviation.
PPS: Purchasing parity standard.

Living alone was associated with an increased probability of

Table 2
Prevalence of worsened mental health during the COVID-19 pandemic in 26 European countries by sociodemographic characteristics and COVID-19 infection status, June–August 2020.

	%	95%CI	p-value	N
Gender				
Male	20.7	19.2–22.3	P < 0.0001 [a]	4,278
Female	34.4	33.1–35.7		9,133
Age group				
50-64	28.1	26.2–30.1	p = 0.279 °	3,956
65-79	27.1	26.1–27.9		6,821
80+	30.6	29.0–32.2		2,634
Respondent had a COVID-19 positive test				
Yes	41.7	29.2–54.2	p = 0.021 [a]	95
No	28.0	27.0–29.1		13,314
Someone close to respondent had a COVID-19 positive test				
Yes	33.5	28.7–38.4	p = 0.014 [a]	1,118
No	27.6	26.6–28.6		12,204
Make ends meet during pandemic				
With great difficulty	38.9	35.6–42.4	P < 0.0001 °	1,742
With some difficulty	31.9	29.6–34.1		3,763
Fairly easily	26.2	24.5–27.8		4,330
Easily	25.0	23.2–26.9		3,276

[a] Chi-square test for proportions; °Chi-square test for trend.

reporting mental health deterioration compared to living in a household with two or more people (1.6 ppt, 95% CI: 0.1–3.1).

Turning to economic risk factors, we observed that job loss and financial difficulty were associated with worsening mental health. We estimated that those who lost their job were 6.5 ppt (95% CI: 1.1–11.8) more likely to report worsened mental health compared with those who did not become unemployed or were already retired. We did not find that having being working or not before the pandemic had an effect on worsening mental health (−1.4 ppt, 95% CI: 3.7–0.9). Finally, those who reported some or great difficulty making ends meet had 5.1 ppt higher risk of worsening mental health (95% CI: 2.9–7.2) compared with those who did not have problems in this regard.

Thus, we found that the risk factors for worsened mental health with the greatest effect sizes were poor and fair self-rated health before the pandemic (21.3 ppt, 95% CI: 17.6–25.0; and 14.6 ppt, 95% CI: 11.2–18.1, respectively), foregone healthcare during the pandemic (14.2 ppt, 95% CI: 12.0–16.5), being female (12.7 ppt, 95% CI: 9.2–16.2), having tested positive for COVID-19 (12.5 ppt, 95% CI: 0.7–24.3), job loss (6.5 ppt, 95% CI: 1.1–11.8), good self-rated health before the pandemic (5.8 ppt, 95% CI: 2.2–9.4), some/great difficulty to make ends meet (5.1 ppt, 95% CI: 2.9–7.2), and living alone (1.6 ppt, 95% CI: 0.1–3.1). After adjusting for other risk factors, we found being aged 80 years old and older vs 50–64 years old (−4.1 ppt, 95% CI: 0.7 to −7.5) had a protective effect.

3.3. Country-level determinants of worsened mental health during the COVID-19 pandemic

Table 4 shows estimates of the impact on worsened mental health of the national toll of COVID-19 cases and of the stringency of policy responses to the pandemic. Countries with a higher number of COVID-19 cases had a greater risk of mental health deterioration (3.1 ppt, 95% CI: 2.3–3.9 per 1,000 cases increase). Next, we found that a higher overall stringency index was associated with a 0.2 ppt (95% CI: 0.1–0.3) increase in the probability of worsened mental health. Several components of the index had specific impacts on mental health deterioration, including workplace closures (6.6 ppt, 95% CI: 2.2–10.9), restrictions on gatherings (3.9 ppt, 95% CI: 0.8–6.9), public transportation closures (6.3 ppt; 95% CI: 2.3–10.2), and stay-at-home requirements (3.1 ppt, 95% CI: 0.6–5.7). We found that greater restrictions on international travel had a protective effect on mental health (−5.1 ppt, 95% CI: 1.7–8.5). No effect on mental health was found for components measuring the cancellation of public events (2.7 ppt, 95% CI: 2.4–3.1), the level of restrictions on national travel (−0.2 ppt, 95% CI: 2.5–2.0) and school closures (0.1 ppt, 95% CI: 2.9–3.1).

Table 3
Individual-level determinants of change in the probability of worsened mental health during the COVID-19 pandemic in 26 European countries, June–August 2020.

	Worsened mental health during the COVID-19 pandemic		
	Model 1	Model 2	Model 3
Age group			
50-64	reference	reference	reference
65-79	−0.00947 (-0.0481–0.0292)	−0.0308* (-0.0615 to −0.0000496)	−0.0292 (-0.0721–0.0138)
80+	0.00418 (-0.0247–0.0330)	−0.0469*** (-0.0664 to −0.0273)	−0.0411* (-0.0750 to −0.00719)
Gender			
Male	reference	reference	reference
Female	0.137*** (0.106–0.169)	0.129*** (0.0964–0.162)	0.127*** (0.0922–0.162)
Self-rated health before pandemic			
Excellent		reference	reference
Very good		0.0176 (-0.0103–0.0454)	0.0134 (-0.0185–0.0453)
Good		0.0661*** (0.0313–0.101)	0.0579** (0.0221–0.0938)
Fair		0.161*** (0.129–0.193)	0.146*** (0.112–0.181)
Poor		0.232*** (0.198–0.266)	0.213*** (0.176–0.250)
Respondent COVID-19 positive			
Not positive		reference	reference
Positive		0.112 (-0.00427–0.229)	0.125* (0.00706–0.243)
Anyone known COVID-19 positive			
No		reference	reference
Yes		0.0260 (-0.0224–0.0743)	0.0288 (-0.0193–0.0769)
Forgone healthcare during pandemic			
No		reference	reference
Yes		0.145*** (0.122–0.168)	0.142*** (0.120–0.165)
Living alone			
2 or more in household			reference
1 person in household (living alone)			0.0162* (0.00128–0.0312)
Make ends meet during pandemic			
Easily/Fairly easily			reference
With some/great difficulty			0.0508*** (0.0293–0.0724)
Working before pandemic			
No or Retired			reference
Yes			−0.0141 (-0.0370–0.00878)
Became unemployed during pandemic			
No or Retired			reference
Yes			0.0646* (0.0110–0.118)
Number of individuals	50278	49856	48566
R^2	0.048	0.079	0.083

95% confidence intervals in brackets.
$^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.
Robust standard errors clustered by country; constant calculated but not shown; all models adjusted by country indicator variables.

Table 5 shows estimates of the association between a series of variables measuring expenditures on social protection benefits and worsened mental health, adjusting for the total number of COVID-19 cases

Table 4

Impact of stringency of policy responses to the pandemic on the change in the probability of worsened mental health during the COVID-19 pandemic in 26 European countries, June–August 2020.

	Worsened mental health during the COVID-19 pandemic	
	Model 1	Models 2-9
Total COVID-19 cases per million inhabitants	0.0000313*** (0.0000234–0.0000392)	
Stringency index of policy responses to the pandemic	0.00237** (0.000895–0.00384)	
Stringency index components:		
C1 School closing		0.000541 (-0.0294–0.0305)
C2 Workplace closing		0.0655** (0.0222–0.109)
C3 Cancel public events		0.0268 (-0.0237–0.0773)
C4 Restrictions on gathering size		0.0387* (0.00830–0.0690)
C5 Close public transport		0.0626** (0.0232–0.102)
C6 Stay at home requirements		0.0311* (0.00560–0.0567)
C7 Restrictions on internal movement		−0.00248 (-0.0250–0.0200)
C8 Restrictions on international travel		−0.0514** (-0.0854–0.0174)
Number of individuals	48566	48566
Number of countries	26	26
R^2	0.077	–

95% confidence intervals in brackets.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

Constant calculated but not shown.

Models 1–9 are adjusted for all variables included in Model 3, Table 2.

Models 2–9 are adjusted for total COVID-19 cases per million inhabitants.

C: component.

Table 5

Impact of social protection expenditures on the change in the probability of worsened mental health during the COVID-19 pandemic in 26 European countries, June–August 2020.

	Worsened mental health during the COVID-19 pandemic	
	Models 1-9	
	Sample	
Per 1,000 € increase in social protection expenditures per capita	*All* (n = 49880)	−0.00339 (-0.00760–0.000829)
	Poor/fair health (n = 16523)	−0.00787* (-0.0155 to −0.000261)
	Unemployed (n = 1888)	−0.0233** (-0.0407 to −0.00592)
	≥65 years old (n = 35292)	−0.00499** (-0.00826 to −0.00172)
	Difficulty make ends meet (n = 17423)	0.00198 (-0.00767–0.0116)
Per 1,000 € increase in health care/ sickness expenditures per capita	*All* (n = 49880)	−0.0130* (-0.0230 to −0.00311)
	Poor/fair health (n = 16523)	−0.0219* (-0.0404 to −0.00340)
Per 1,000 € increase in unemployment benefits expenditures per capita	*Unemployed* (n = 1888)	−0.380* (-0.711 to −0.0504)
Per 1,000 € increase in pensions/old age expenditures per capita	*≥65 years old* (n = 35292)	0.00375 (-0.00598–0.0135)

95% confidence intervals in brackets.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

Constant calculated but not shown.

All models adjusted by age, gender, health status before the pandemic, tested positive for COVID-19 oneself or someone close, household size, total COVID-19 cases per million inhabitants, and stringency index of policy responses to the pandemic.

and stringency of policy responses. For each additional €1,000 increase in expenditures on overall social protection benefits, reporting of worsened mental health decreased among those who became unemployed during the pandemic (−2.3 ppt, 95% CI: 0.6–4.1), individuals with poor/fair health (−0.8 ppt, 95% CI: 0.01–1.5), and among individuals aged ≥65 years (−0.5 ppt, 95% CI: 0.2–0.8). No effect of overall social protection spending was observed the population in general (−0.3 ppt, 95% CI: 0.7–0.1) and those facing difficulties making ends meet (0.2 ppt, 95% CI: 0.7–1.2). The same increase in spending on healthcare was associated with a protective effect on the mental health of the general population (−1.3 ppt, 95% CI: 0.3–2.3) and a stronger effect among those who reported poor health (−2.2 ppt, 95% CI: 0.3–4.0). In countries with higher spending on unemployment benefits, worsened mental health among the unemployed was ameliorated (−3.8 ppt, 95% CI: 0.5–7.1 per €100 increased spending; here, as opposed to Table 5, we report changes per €100 instead of €1,000 because the range of amounts paid in unemployment benefits among countries is substantially lower than for other social protection payments, as shown in Table 1). Differences in pension spending were not associated with the probability of reporting adverse mental health among people aged ≥65 (0.4 ppt, 95% CI: 0.6–1.4 per €1,000 increase in spending).

3.4. *Sensitivity tests*

We ran a series of sensitivity tests using the two components of the main outcome as outcome variables: worsened depression and worsened anxiety since the inception of the COVID-19 pandemic, observing that the findings did not substantially change, although in some instances the estimates' effect sizes were smaller or greater than with the combined outcome (Online supplementary material).

4. Discussion

We found a substantial deterioration in mental health in persons aged 50 years and older between the beginning of the pandemic and June to August 2020. This was strongly associated with greater severity of physical distancing measures and exhibited substantial social inequalities, with people with poor and fair health, foregoing healthcare, women, and persons who experienced job loss and financial hardship during the pandemic suffering the most. Importantly, however, stronger social protection systems, as measured by greater spending, appeared to mitigate the risk of worsened mental health.

We observed great differences across countries in the prevalence of worsened mental health, again consistent with previous research (Wang et al., 2020). However, a consistent finding is that people in lower socioeconomic groups and women have been hardest hit. Individuals with worse overall health status before the pandemic were substantially more likely to experience mental health deterioration, as were individuals with unmet healthcare needs since the inception of the pandemic. This might suggest a relationship between COVID-19 comorbidities and deteriorating mental health. Also, those with a diagnosis of COVID-19 were more likely to experience further declines in mental health, which is aligned with findings from previous research (Taquet et al., 2021a, 2021b). This could be due to, or exacerbated by, fear of becoming severely ill or dying as well as disrupted health services provision (World Health Organization, 2020a), including reduced access to mental health services, either for ongoing conditions or for new ones arising since the inception of the pandemic.

Individuals who reported good overall health status during the pandemic also experienced declines in mental health, which may be due not only to COVID-19, but also the physical distancing measures and closure policies having impacted mental health, particularly through job loss and difficulties to make ends meet. In this context, greater social protection expenditures may have increased resilience during the pandemic as our social protection variable was measured pre-pandemic. That the expenditures measures are pre-pandemic might also explain why we found greater expenditures in a full package of social protection protected the mental health for some population subgroups (those with poor health, unemployed, and those aged 65 and older, all of who may have benefited from a stronger public health system, unemployment benefits, and old age pensions); however, greater expenditures in a full package of social protection did not protect the mental health of the whole population aged 50 years old and older as many may have not been directly benefiting from the social protection programmes until after the crisis began.

Our analysis has several limitations. First, we were unable to attribute worsened mental health with certainty to the pandemic and policy responses or some other event during this time frame. However, the outcome variable is based on a question inquiring whether mental health had worsened since the onset of the pandemic, which is likely to anchor it to the pandemic. While SHARE is a panel dataset, the timing of the wave, in summer 2020, means that we have no absolute measure of mental health just prior and subsequent to the onset of the pandemic but the additional question in the cross-sectional data, asking whether symptoms had worsened since the inception of the pandemic partially circumvents this limitation. Nonetheless, other studies using longitudinal designs have produced similar findings to ours (Ettman et al., 2020; González-Sanguino et al., 2020; Pan et al., 2021; M.; Pierce, Hope, et al., 2020). Although we were not able to adjust for previous mental health status specifically, we could adjust for prior self-reported general health status.

A second limitation is the ecologic nature of the social protection measures used in the analysis. Thus, we could not include individual level data on social protection benefits although we could identify those potentially eligible for pensions or unemployment benefits. Third, we did not include data on other socioeconomic determinants of mental health, such as experience of racism among migrants and minority ethnic groups. Also, while almost everyone in Europe is affected by the pandemic, we were not able to capture aspects that may have made individual exposure to it more or less intense. Fourth, mental health can be complex to measure. We used self-reported data where response bias could have over or underestimated the strength of the associations. However, self-reporting is common in mental health research. Telephone interviewing could have also made respondents hesitant to accurately report information, particularly mental health and financial status information. Measurement of social protection systems is difficult, and our measurement approach is just an approximation. While the Oxford COVID-19 government response tracker aims to capture how many measures a government has adopted and to what degree, the index cannot say whether each has been effectively implemented and whether it is adhered to. Differences in policy implementation and adherence could have biased our estimates, over or under-estimating the strength of the reported associations. Fifth, the findings herein refer to the first few months of the pandemic, as the data were collected between June and August 2020 but the relationship between social protection and mental health may change over time, particularly when assessing social protection measures introduced during the pandemic as opposed to assessing previously established social protection systems as we have done. Finally, our study only included the population aged 50 and above, so the findings cannot be extrapolated to the rest of the population. Most other studies have focused on younger populations (adolescents, university students) and healthcare workers. Thus, our study fills an important gap, capturing experiences of those hardest hit by COVID-19 illness. Although we would expect similar findings, further research could explore the impact of the COVID-19 pandemic on mental health among older populations in low- and middle-income countries.

Our study has implications for policy. It reveals how the adverse impacts of physical distancing and closures are not inevitable. Increased spending on various social protection benefits, including healthcare, unemployment, and a package of social protection benefits seems to ameliorate the risk of mental health deterioration. A recent study found that governments in many countries were perceived to have responded poorly to the burden of mental health suffering associated with COVID-19 (Lazarus et al., 2020). Greater expenditure on social protection may have enabled more support and acted as a safety net for those at risk of mental health problems during what was a health and economic crisis. These findings are consistent with the aforementioned study from the United States which found that stronger social support policies helped mitigate the mental health consequences of household income shocks during the COVID-19 pandemic (Donnelly & Farina, 2021). We also found that individuals living alone had a higher risk of mental health deterioration, which may be explained by feelings of isolation and lack of social support, particularly among older people who may have less access to digital communications. This highlights the importance of considering emotional and social support as part of government and civil society responses to the COVID-19 pandemic, bearing in mind that many of those worst affected risk being further excluded from the increasingly digital delivery of services (Seifert et al., 2021). Faced with a continuing COVID-19 pandemic, with more time spent under physical distancing and other containment measures and further economic downturn, there is a risk of further harm to mental health. It is imperative that countries build strong social protection systems and resilient health systems that can protect their populations from the mental health consequences of crises (Hanefeld et al., 2018; Tediosi et al., 2020; Thomas et al., 2020; World Health Organization, 2020a).

Author statement

AML conceived the study, analysed the data, and prepared the first draft. AML and DS designed the study. All authors provided critical revisions and contributed to the interpretation of the data and writing of the manuscript. All authors read and approved the submitted manuscript.

Data sharing

SHARE data is available upon registration on their website. Data from Eurostat and from the Oxford COVID-19 Government Response Tracker are publicly available on their websites.

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Ethical statement

Hereby, I, Ana Méndez López, consciously assure that for the manuscript submitted the following is fulfilled:

1) This material is the authors’ own original work, which has not been previously published elsewhere.
2) The paper is not currently being considered for publication elsewhere.
3) The paper reflects the authors’ own research and analysis in a truthful and complete manner.

4) The paper properly credits the meaningful contributions of co-authors and co-researchers.
5) The results are appropriately placed in the context of prior and existing research.
6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2021.101017.

References

Bergmann, M., Kneip, T., De Luca, G., & Scherpenzeel, A. (2019). *Survey participation in the survey of health, ageing and retirement in Europe (SHARE), wave 1-7. Based on release 7.0.0*. SHARE-ERIC.

Börsch-Supan, A. (2020). *Survey of health, ageing and retirement in Europe (SHARE) wave 8. COVID-19 survey 1. Release version: 0.0.1. Beta*. SHARE-ERIC.

Börsch-Supan, A., Brandt, M., Hunkler, C., Kneip, T., Korbmacher, J., Malter, F., et al. (2013). Data resource profile: The survey of health, ageing and retirement in Europe (SHARE). *International Journal of Epidemiology, 42*, 992–1001.

Brooks, S. K., Webster, R. K., Smith, L. E., Woodland, L., Wessely, S., Greenberg, N., et al. (2020). The psychological impact of quarantine and how to reduce it: Rapid review of the evidence. *Lancet, 395*, 912–920.

Dong, E., Du, H., & Gardner, L. (2020). An interactive web-based dashboard to track COVID-19 in real time. *The Lancet Infectious Diseases, 20*, 533–534.

Donnelly, R., & Farina, M. P. (2021). How do state policies shape experiences of household income shocks and mental health during the COVID-19 pandemic? *Social Science & Medicine, 269*, Article 113557.

Ettman, C. K., Abdalla, S. M., Cohen, G. H., Sampson, L., Vivier, P. M., & Galea, S. (2020). Prevalence of depression symptoms in US adults before and during the COVID-19 pandemic. *JAMA Network Open, 3*, Article e2019686.

Eurostat. (2021). *European system of integrated social PROtection statistics (ESSPROS)*.

Fancourt, D., Steptoe, A., & Bu, F. (2021). Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in england: A longitudinal observational study. *The Lancet Psychiatry, 8*, 141–149.

González-Sanguino, C., Ausín, B., Castellanos, M., Saiz, J., López-Gómez, A., Ugidos, C., et al. (2020). Mental health consequences during the initial stage of the 2020 Coronavirus pandemic (COVID-19) in Spain. *Brain, Behavior, and Immunity, 87*, 172–176.

Hale, T., Angrist, N., Goldszmidt, R., Kira, B., Petherick, A., Phillips, T., et al. (2021). A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nature Human Behaviour, 5*, 529–538.

Hanefeld, J., Mayhew, S., Legido-Quigley, H., Martineau, F., Karanikolos, M., Blanchet, K., et al. (2018). Towards an understanding of resilience: Responding to health systems shocks. *Health Policy and Planning, 33*, 355–367.

Holmes, E. A., O'Connor, R. C., Perry, V. H., Tracey, I., Wessely, S., Arseneault, L., et al. (2020). Multidisciplinary research priorities for the COVID-19 pandemic: A call for action for mental health science. *The Lancet Psychiatry, 7*, 547–560.

Lazarus, J. V., Ratzan, S., Palayew, A., Billari, F. C., Binagwaho, A., Kimball, S., et al. (2020). COVID-SCORE: A global survey to assess public perceptions of government responses to COVID-19 (COVID-SCORE-10). *PLoS One, 15*, Article e0240011.

Lloyd-Sherlock, P., Ebrahim, S., Geffen, L., & McKee, M. (2020). Bearing the brunt of covid-19: Older people in low and middle income countries. *BMJ, 368*, m1052.

Pan, K.-Y., Kok, A. A. L., Eikelenboom, M., Horsfall, M., Jörg, F., Luteijn, R. A., et al. (2021). The mental health impact of the COVID-19 pandemic on people with and without depressive, anxiety, or obsessive-compulsive disorders: A longitudinal study of three Dutch case-control cohorts. *The Lancet Psychiatry, 8*, 121–129.

Pierce, M., Hope, H., Ford, T., Hatch, S., Hotopf, M., John, A., et al. (2020a). Mental health before and during the COVID-19 pandemic: A longitudinal probability sample survey of the UK population. *The Lancet Psychiatry, 7*, 883–892.

Pierce, M., McManus, S., Jessop, C., John, A., Hotopf, M., Ford, T., et al. (2020b). Says who? The significance of sampling in mental health surveys during COVID-19. *The Lancet Psychiatry, 7*, 567–568.

Richardson, R. A., Keyes, K. M., Medina, J. T., & Calvo, E. (2020). Sociodemographic inequalities in depression among older adults: Cross-sectional evidence from 18 countries. *The Lancet Psychiatry, 7*, 673–681.

Seifert, A., Cotten, S. R., & Xie, B. (2021). A double burden of exclusion? Digital and social exclusion of older adults in times of COVID-19. *Journal of Gerontology: Serie Bibliographique, 76*, e99–e103.

Sounderajah, V., Clarke, J., Yalamanchili, S., Acharya, A., Markar, S. R., Ashrafian, H., et al. (2021). A national survey assessing public readiness for digital health strategies against COVID-19 within the United Kingdom. *Scientific Reports, 11*, 5958.

StataCorp. (2019). *Stata statistical software: Release 16*. College Station, TX: StataCorp LP.

Taquet, M., Geddes, J. R., Husain, M., Luciano, S., & Harrison, P. J. (2021a). 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: A retrospective cohort study using electronic health records. *The Lancet Psychiatry*.

Taquet, M., Luciano, S., Geddes, J. R., & Harrison, P. J. (2021b). Bidirectional associations between COVID-19 and psychiatric disorder: Retrospective cohort studies of 62354 COVID-19 cases in the USA. *The Lancet Psychiatry, 8*, 130–140.

Tediosi, F., Lönnroth, K., Pablos-Méndez, A., & Raviglione, M. (2020). Build back stronger universal health coverage systems after the COVID-19 pandemic: The need for better governance and linkage with universal social protection. *BMJ Glob Health, 5*.

Thomas, S., Sagan, A., Larkin, J., Cylus, J., Figueras, J., & Karanikolos, M. (2020). *Strengthening health systems resilience: Key concepts and strategies*. European Observatory Policy Briefs Copenhagen (Denmark): European Observatory on Health Systems and Policies, World Health Organization 2020 (acting as the host organization for, and secretariat of, the European Observatory on Health Systems and Policies).

United Nations Secretary-General Policy Brief. (2020). *United Nations policy Brief: COVID-19 and the need for action on mental health*. New York, NY, USA: United Nations.

Vahia, I. V., Jeste, D. V., & Reynolds, C. F., 3rd (2020). Older adults and the mental health effects of COVID-19. *JAMA, 324*, 2253–2254.

Vindegaard, N., & Benros, M. E. (2020). COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain, Behavior, and Immunity, 89*, 531–542.

Wang, Y., Kala, M. P., & Jafar, T. H. (2020). Factors associated with psychological distress during the coronavirus disease 2019 (COVID-19) pandemic on the predominantly general population: A systematic review and meta-analysis. *PLoS One, 15*, Article e0244630.

World Health Organization. (2020a). *Health inequity and the effects of COVID-19: Assessing, responding to and mitigating the socioeconomic impact on health to build a better future*. World Health Organization. Regional Office for Europe.

World Health Organization. (2020b). *Listings of WHO's response to COVID-19*.

World Health Organization. (2020c). *Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March 2020*. World Health Organization.

Xiong, J., Lipsitz, O., Nasri, F., Lui, L. M. W., Gill, H., Phan, L., et al. (2020). Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *Journal of Affective Disorders, 277*, 55–64.

3. Summary of findings, discussions, and conclusions

Overall, these five studies highlight the complex interplay of social, behavioural, and structural factors in the resurgence of syphilis among MSM in Europe, the effectiveness of earlier HIV treatment initiation, the persistent presence of HIV stigma and its impact on testing uptake, and the importance of social protection systems in supporting mental health during crises. The conclusions from the studies highlight the crucial role of social determinants of health in shaping health outcomes. These findings emphasize two key points. Firstly, they underscore the significance of addressing modifiable risk factors associated with social determinants, such as socioeconomic disparities, healthcare accessibility, and health and socioeconomic policies, to enhance population health and promote health equity. Secondly, the results suggest that adopting a comprehensive approach that addresses both micro- and macro-level social, behavioural, and structural determinants of health can result in improved health outcomes and contribute to the development of more equitable societies.

Study 1:

- The study shows a significant increase in self-reported syphilis diagnoses among MSM participating in the study. Syphilis diagnoses are concentrated in three MSM population groups: HIV-diagnosed, PrEP users, and sex workers. The rise in syphilis diagnoses has disproportionately affected HIV-diagnosed MSM and MSM sex workers.

- More recent STIs screening and an increased number of non-steady male CAI partners are major determinants associated with syphilis diagnoses. These factors mediate the association between PrEP use and a higher chance of syphilis diagnosis. The number of non-steady male CAI partners is suggested to be a mediator between PrEP use and higher odds of syphilis diagnosis, but the study cannot determine if individuals using PrEP already had higher numbers of non-steady male CAI partners before initiating PrEP.

- Recency of STIs screening plays a key role in syphilis diagnoses. MSM who reported being screened for STIs more recently also reported higher numbers of non-steady male CAI partners, indicating more syphilis screening among MSM with riskier sexual behavior, including PrEP users, HIV-diagnosed individuals, and people involved in sex work.

- Clinical implications include offering syphilis screening to MSM with multiple CAI partners due to their increased risk. Guidelines for PrEP users should include regular syphilis screening, and community-based education is needed to increase knowledge and social norms regarding syphilis screening. Additional interventions such as online risk assessment tools, home-sampling, free at-point-of-use tests, and partner notification tools are suggested to be considered for national syphilis control and elimination strategies.

Study 2:

- Reports of number of sexual partners in the previous six or 12 months in sexual behaviour surveys for MSM are clustered in the tens (e.g., 10, 20, 30, etc. partners in the previous 12 months), suggesting that partner numbers beyond nine—and irrespective of the chosen timeframe—were best guesses rather than precise counts, with 12, ‘60’, and '120' possibly reflecting 'about one per month', ‘about five per month’, and 'about ten per month', respectively, in a twelve months retrospective period.

- When using data from quantitative discrete scale variables (e.g. counts of 1, 2, 3, 4, etc. partners) for producing means of partner numbers for the categories of qualitative variables (e.g. between 10-20 partners), the difference between means of partner numbers decreased in higher categories when comparing partner numbers in the previous twelve months versus the previous six months. This suggests a cognitive effect known as the telescoping effect, where events are perceived as happening closer or further from the time of the survey, leading to potential biases in the analysis of sexual behaviour data.

- In the highest partner number categories, the distribution of data from the quantitative variables was highly dispersed with wide interquartile ranges and high standard deviations. Adding additional categories in the upper range (e.g., measuring 51-100 / 50-99 sexual partners and 'more than 100' / '100 or more' sexual partners) may improve precision in measuring partner numbers in surveys using categorical variables.

- For categories of partner numbers above nine, the mean numbers of sexual and CAI partners were similar, indicating that non-condom use is more common with larger numbers of sexual partners.

Study 3:

- Stigmatized and discriminatory attitudes towards people with HIV are prevalent in all countries, with varying levels of stigma across different settings. In settings with higher HIV prevalence, reported stigma is commonly lower, possibly due to greater awareness and lived experiences with HIV.

- Sociodemographic characteristics such as lower educational level, lower wealth, being female, and being an adolescent are associated with holding a greater stigma towards people with HIV. Lack of comprehensive knowledge about HIV is a key characteristic associated with stigmatized attitudes towards people with HIV.

- Stigmatized and discriminatory attitudes towards people with HIV are associated with lower HIV testing uptake. This highlights the importance of addressing stigma as a barrier to accessing HIV testing and ultimately ending the HIV epidemic.

- The study emphasizes the need for context-specific and population-specific interventions to reduce stigma towards people with HIV. Interventions should consider the sociodemographic characteristics and prevailing attitudes in each setting. Interventions aimed at eliminating stigma should focus on increasing HIV knowledge, addressing misconceptions, reducing stigma, and promoting understanding and acceptance of individuals living with HIV among individuals and communities. Interventions could include national and community-level campaigns as well as targeted interventions in educational and health settings.

Study 4:

- The findings suggest that adopting test-and-treat policies is associated with greater population-level access to ART and higher rates of viral suppression compared to more restrictive ART initiation policies based on CD4 cell count thresholds. The study indicates that the effect of test-and-treat on expanding ART coverage is likely substantial compared to alternative ART initiation policies. Additionally, earlier treatment initiation at CD4 ≤ 500 cells/mm^3 was associated with a decline in new HIV infections, highlighting the importance of initiating ART at higher CD4 cell count thresholds in reducing transmission rates.

- Expanding access to testing and treatment is the main policy implication. Ensuring widespread availability of HIV testing, as well as accessible and affordable treatment options, is critical for early diagnosis, management, and prevention of transmission. The findings also suggest that achieving the UNAIDS 95-95-95 target, which aims to diagnose 95% of people living with HIV, provide ART to 95% of diagnosed individuals, and achieve viral suppression in 95% of those on ART, and the SDG target for ending the AIDS epidemic can be facilitated by test-and-treat policies and universal access to ART in strengthened health systems.

Study 5:

- There was a significant deterioration in mental health among individuals aged 50 and older during the early months of the COVID-19 pandemic. This deterioration was strongly associated with the severity of physical distancing measures and exhibited social inequalities, with those in poor health, women, individuals with unmet healthcare needs, and individuals experiencing job loss and financial hardship being the most affected. Individuals diagnosed with COVID-19 also experienced further declines in mental health, possibly due to fear of severe illness or disrupted healthcare services.

- Countries exhibited significant variations in the prevalence of worsened mental health during the pandemic. Stronger social protection systems in countries, as indicated by higher spending, appeared to mitigate the risk of worsened mental health during the pandemic.

- The findings suggest that increased spending on social protection benefits, including healthcare, unemployment support, and a comprehensive package of social protection, can help protect against mental health deterioration during times of crisis. It is crucial for countries to build strong social protection systems and resilient health systems to protect populations from the mental health consequences of crises like the COVID-19 pandemic.

Resumen de los resultados, discusiones y conclusiones

En general, estos cinco estudios destacan la compleja interacción de factores sociales, conductuales y estructurales en el resurgimiento de la sífilis entre HSH en Europa, la efectividad de la iniciación temprana del tratamiento del VIH, la persistente presencia del estigma del VIH y su impacto en la realización de pruebas y la importancia de los sistemas de protección social en apoyar la salud mental durante crisis. Las conclusiones de los estudios resaltan el papel crucial de los determinantes sociales de la salud en la formación de los resultados sanitarios. Estos hallazgos enfatizan dos puntos clave. En primer lugar, subrayan la importancia de abordar los factores de riesgo modificables relacionados con los determinantes sociales, como las disparidades socioeconómicas, la accesibilidad a la atención médica y las políticas sanitarias y socioeconómicas para mejorar la salud de la población y promover la equidad en salud. En segundo lugar, los resultados sugieren que adoptar un enfoque integral que aborde los determinantes de salud sociales, conductuales y estructurales tanto a nivel micro como macro puede resultar en un mejor estado de salud y contribuir al desarrollo de sociedades más equitativas.

Estudio 1:

- El estudio muestra un aumento significativo de los diagnósticos de sífilis autoreportados entre los hombres que tienen relaciones sexuales con hombres (HSH) participantes en el estudio. Los diagnósticos de sífilis se concentran en tres grupos de población de HSH: diagnosticados con VIH, usuarios de PrEP y trabajadores sexuales. El aumento de los diagnósticos de sífilis ha afectado de forma desproporcionada a los HSH diagnosticados con VIH y a los trabajadores sexuales HSH.

- El tiempo transcurrido desde la última prueba de detección de ITS y el número de parejas sexuales masculinas no estables en las que hay relaciones anales sin preservativo son los principales determinantes asociados a los diagnósticos de sífilis. Estos factores median en la asociación entre el uso de la PrEP y una mayor probabilidad de diagnóstico de sífilis. Se sugiere que el número de parejas sexuales masculinas no estables en las que hay relaciones anales sin preservativo es un mediador entre el uso de la PrEP y las mayores probabilidades de diagnóstico de sífilis, pero el estudio no puede determinar si los individuos que usan la

PrEP ya tenían un mayor número de parejas sexuales masculinas no estables en las que hay relaciones anales sin preservativo antes de iniciar la PrEP.

- Un menor tiempo transcurrido desde la prueba de ITS más reciente desempeña un papel clave en el diagnóstico de sífilis. Los HSH que declararon haberse hecho pruebas de detección de ITS más recientemente también declararon un mayor número de parejas sexuales masculinas no estables en las que hay relaciones anales sin preservativo, lo que indica un mayor número de pruebas de detección de sífilis entre los HSH con un comportamiento sexual de mayor riesgo, incluidos los usuarios de la PrEP, las personas diagnosticadas con VIH y las personas que ejercen el trabajo sexual.

- Las implicaciones clínicas incluyen ofrecer el cribado de sífilis a los HSH con múltiples parejas sexuales masculinas no estables en las que hay relaciones anales sin preservativo debido a su mayor riesgo. Las directrices para los usuarios de la PrEP deberían incluir el cribado periódico de la sífilis. También es necesaria la educación comunitaria para aumentar el conocimiento y las normas sociales relativas al cribado de la sífilis. Se sugiere que se consideren intervenciones adicionales para las estrategias nacionales de control y eliminación de la sífilis, como herramientas online de evaluación de riesgos, muestreo domiciliario ("home-/self-testing"), pruebas gratuitas en el punto de consumo y herramientas de notificación a la pareja.

Estudio 2:

- Los informes sobre el número de parejas sexuales en los seis o doce meses anteriores en las encuestas sobre conducta sexual para HSH se agrupan en las decenas (por ejemple, 10, 20, 30, etc. parejas sexuales), lo que sugiere que el número de parejas más allá de nueve (e independientemente del marco temporal elegido) eran más bien estimaciones o conjeturas en vez de recuentos precisos. Respuestas indicando "12", "60" y "120" parejas sexuales reflejan posiblemente "alrededor de una al mes", "alrededor de cinco al mes" y "alrededor de diez al mes", respectivamente, en un periodo retrospectivo de doce meses.

- Se utilizan datos de variables cuantitativas de escala discreta (por ejemplo, datos de conteo o recuento del número de parejas sexuales tales como 1, 2, 3, etc. parejas sexuales) para producir medias de números de parejas sexuales para sustituir con estos valores las categorías de variables cualitativas (por ejemplo, ‘entre 10-20 parejas sexuales). Al comparar la media del número de parejas sexuales entre el marco temporal de los últimos 12 meses y los últimes seis meses, se observa que la diferencia entre medias de números de parejas disminuye en las categorías más altas (es decir, en las categorías que miden 20, 30, 40 o 50 parejas sexuales). Esto sugiere un efecto cognitivo conocido como efecto telescopio, en el que los acontecimientos se perciben como ocurridos más cerca o más lejos del momento de la encuesta, lo que conduce a posibles sesgos en el análisis de los datos de comportamiento sexual.

- En las categorías más altas del número de parejas (es decir, en las categorías que miden 20-30, 30-40, 40-50 o >50 parejas sexuales), la distribución de los datos de las variables cuantitativas fue muy dispersa, con amplios rangos intercuartílicos y altas desviaciones típicas. Añadir categorías adicionales en el rango superior (por ejemplo, medir 51-100 / 50-99 parejas sexuales y "más de 100" / "100 o más" parejas sexuales) puede mejorar la precisión en la medición del número de parejas en las encuestas que utilizan variables categóricas.

- Para las categorías de número de parejas superiores a nueve, los números medios de parejas sexuales (en general) y parejas sexuales con relaciones anales sin preservativo fueron similares, lo que indica que el uso de preservativos es inferior entre aquellas personas con un mayor número de parejas sexuales.

Estudio 3:

- Las actitudes estigmatizantes y discriminatorias hacia las personas con VIH son frecuentes en todos los países, aunque con diferente nivel según el país. En los entornos con una mayor prevalencia del VIH, el estigma declarado suele ser menor, posiblemente debido a un mayor conocimiento del VIH y a las experiencias vitales con el VIH.

- Las características sociodemográficas, como un menor nivel educativo, una menor riqueza, el hecho de ser mujer y ser adolescente, se asocian a una mayor estigmatización de las personas con VIH. La falta de conocimientos amplios sobre el VIH es una característica clave asociada a las actitudes estigmatizantes hacia las personas con HIV.

- Las actitudes estigmatizantes y discriminatorias hacia las personas con VIH se asocian a una menor realización de la pruebas del VIH. Esto pone de relieve la importancia de abordar el estigma como una barrera para acceder a las pruebas del VIH y, en última instancia, acabar con la epidemia del VIH.

- El estudio subraya la necesidad de intervenciones específicas para cada contexto y población con el fin de reducir el estigma hacia las personas con VIH. Las intervenciones deben tener en cuenta las características sociodemográficas y las actitudes predominantes en cada entorno. Las intervenciones dirigidas a eliminar el estigma deben centrarse en aumentar los conocimientos sobre el VIH, abordar las ideas erróneas, reducir el estigma y promover la comprensión y la aceptación de las personas que viven con el VIH tanto a nivel individuals como a nivel comunitario. Las intervenciones podrían incluir campañas nacionales y comunitarias, así como intervenciones específicas en entornos educativos y sanitarios.

Estudio 4:

- Los resultados sugieren que la adopción de guías de tratamiento del VIH que recomienden "prueba y tratamiento" (‘test-and-treat’) se asocia con un mayor acceso de la población a la terapia antirretroviral (TAR) y mayores tasas de supresión vírica en comparación con las políticas más restrictivas de inicio de la TAR basadas en umbrales de recuento de células CD4. El estudio indica que el efecto de políticas ‘test-and-treat’ en la ampliación de la cobertura de la terapia antirretroviral es probablemente sustancial en comparación con otras políticas alternativas de inicio de la terapia antirretroviral. Además, el inicio más temprano del tratamiento con un recuento de CD4 ≤500 células/mm^3 se asoció a un descenso de las nuevas infecciones por el VIH, lo que pone de relieve la importancia de iniciar la terapia antirretroviral en umbrales de recuento de CD4 más altos para reducir las tasas de transmisión.

- Ampliar el acceso a las pruebas y el tratamiento es la principal implicación política. Garantizar la disponibilidad generalizada de pruebas de VIH, así como opciones de tratamiento accesibles y asequibles, es fundamental para el diagnóstico temprano, la gestión y la prevención de la transmisión. Los hallazgos también sugieren que se puede facilitar el logro del objetivo 95-95-95 de ONUSIDA, que tiene como objetivo diagnosticar al 95% de las personas que viven con el VIH, proporcionar tratamiento antirretroviral al 95% de los diagnosticados y lograr la supresión viral en el 95% de quienes reciben tratamiento antirretroviral, así como el objetivo de los Objetivos de Desarrollo Sostenible (ODS) de poner fin a la epidemia de SIDA, mediante políticas de prueba y tratamiento y el acceso universal al tratamiento antirretroviral en sistemas de sanitarios fortalecidos.

Estudio 5:

- Durante los primeros meses de la pandemia COVID-19 se produjo un deterioro significativo de la salud mental entre las personas de 50 años o más. Este deterioro estuvo fuertemente asociado a la gravedad de las medidas de distanciamiento físico y mostró desigualdades sociales, siendo los más afectados los individuos que reportaron tener mala salud previamente, las mujeres, los individuos con necesidades sanitarias no cubiertas y los individuos que experimentaron pérdida de empleo y dificultades económicas. Las personas diagnosticadas con COVID-19 también experimentaron un mayor deterioro de la salud mental, posiblemente debido al temor a una enfermedad grave o a la interrupción de los servicios sanitarios.

- Los países mostraron variaciones significativas en la prevalencia del empeoramiento de la salud mental durante la pandemia. Los sistemas de protección social nacionales más sólidos, indicado por el aumento del gasto público, parecieron mitigar el riesgo de empeoramiento de la salud mental durante la pandemia.

- Los resultados sugieren que un mayor gasto en prestaciones de protección social, incluida la asistencia sanitaria, las ayudas al desempleo y un paquete integral de protección social, puede ayudar a proteger contra el deterioro de la salud mental en tiempos de crisis. Es crucial que los países construyan sistemas de protección social sólidos y sistemas sanitarios resilientes para proteger a la población de las consecuencias para la salud mental de crisis como la pandemia de COVID-19.

4. Appendix

Supplemental data Study 1

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Appendix 1. EMIS survey details: additional information for recruitment and included variables

Data source:

EMIS was available in 25 languages in 2010 and 33 languages in 2017. The 2017 wave differed principally from 2010 by including the use of smartphone apps (65.8% of the 2017 analytic sample), which had become commonplace across all countries surveyed. Recruitment took place through promotion via supportive organisations within the EMIS network (national/trans-national, civil society, HIV/LGBT groups, *etc.*), accounting for 20.7% of recruits in EU/EFTA countries in 2010, and for 15.6% of recruits in 2017—often using social networking sites (Facebook, Twitter and Instagram). In both waves, however, the majority of recruits came via direct message invitations and advertising on geo-spatial dating websites and smartphone applications (79.0% in 2010, 79.6% in 2017, the most prominent being PlanetRomeo in both waves, the second most prominent in 2017 being Grindr with 21.4%). The 2017 response rate in EU/EFTA countries was 6.6 per 10,000 men aged 15–65, ranging from 3.0 in Poland to 20.1 in Malta. The survey designers suggest that this figure roughly translates to 2.3% of all MSM in EU/EFTA countries. Further details about the data are provided in the EMIS design and methods papers.[1,2] More information can also be found in the EMIS website: www.emis2017.eu.

Discrepant data:

Discrepancies in data arise if answers to two or more questions are logically inconsistent for any of three key variables: age, steady male partners and non-steady partners, each with seven, five and six possible inconsistencies respectively; if a case had at least one inconsistency in any of these three areas, it was flagged as discrepant (n=35,859, 12.89% of the sample). In robustness checks, discrepant cases were excluded.

Variables:

Educational level: In EMIS-2010, the classification for the variable education was done according to levels of the International Classification of Education (ISCED) from 1997, where ISCED 1 corresponds to the lowest level of education of the scale (primary education) and ISCED 6 corresponds to the higher level of education (second stage tertiary education, *e.g.*, PhD). In EMIS-2017, we instead asked for the years spent in full-time education since the age of 16. How these years can be converted into ISCED categories differs across time and across countries. For the sake of comparability, we consulted a manual published by the Organisation for Economic Co-development and Development (OECD), to convert the new measure into ISCED levels (Organisation for Economic Co-operation and Development: *Classifying Educational Programmes. Manual for ISCED-97 Implementation in OECD Countries*. Paris, 1999). Very broadly speaking, 2–5 years of education beyond 16 years correspond to an ISCED-97 level three (upper secondary education); 6 years or more correspond to an ISCED-97 level five (first stage of tertiary education), and more than 10 years correspond to an ISCED-97 level six (second stage of tertiary education). In this study educational categories low, mid and high correspond to the following 1997 ISCED levels: Low: ISCED 1–2; Mid: ISCED 3–4; and High: ISCED 5–6. Further details about the data are provided in the EMIS design and methods papers.[1,2] More information can also be found in the EMIS website: www.emis2017.eu.

Number of steady and non-steady [CAI] partners: These variables were collected as discrete with intervals for higher number of partners and truncated for the category at the top end, i.e. 1, 2, 3… 8, 9, and 10+ (steady male partners), or 1, 2, 3…8, 9, 10, 11–20, 21–30, 31–40, 41–50, and more than 50 (non-steady male partners). Numeric substitutes for each of the interval and truncated categories are based on findings from a meta-analysis.[3] They were rounded to the nearest decimal when used in hierarchical negative binomial models. Nonetheless, estimates of the impact of these variables on risk of syphilis diagnosis are also provided using the variables in their original categorical format (see Figure 3).

Sub-optimal translation syphilis diagnosis question in French questionnaire and adjustment:
The sub-optimal translation of the syphilis diagnosis question in the French language questionnaire in 2017 occurred because the way in which it was asked may have made some respondents think that they were being surveyed about whether they had a syphilis diagnostic test performed instead of being diagnosed with syphilis. Therefore, although technically correct, this wording in the French questionnaire has probably inflated the number of people reporting a positive answer to the question. The exact lead-in question was *"Have you ever been diagnosed with syphilis?"*, and in French "*Avez-vous déjà eu un diagnostic de syphilis*?" (2017) vs. "*Avez-vous déjà eu un diagnostic positif de syphilis?"* (2010)
A total of 10.8% of the study sample used the French version of the questionnaire in 2017. The countries mostly affected were France (with 93.3% of respondents using the French questionnaire), Belgium (35.9%), Luxembourg (27.2%), and Switzerland (19.2%).
We adjusted all statistical analyses for this translation using a dichotomous variable to indicate whether the questionnaire of 2017 language was French as in 2010 the wording was not misleading. Further

details about the data source are provided in the EMIS design and methods papers.1,2 More information can also be found in the EMIS website: www.emis2017.eu

References

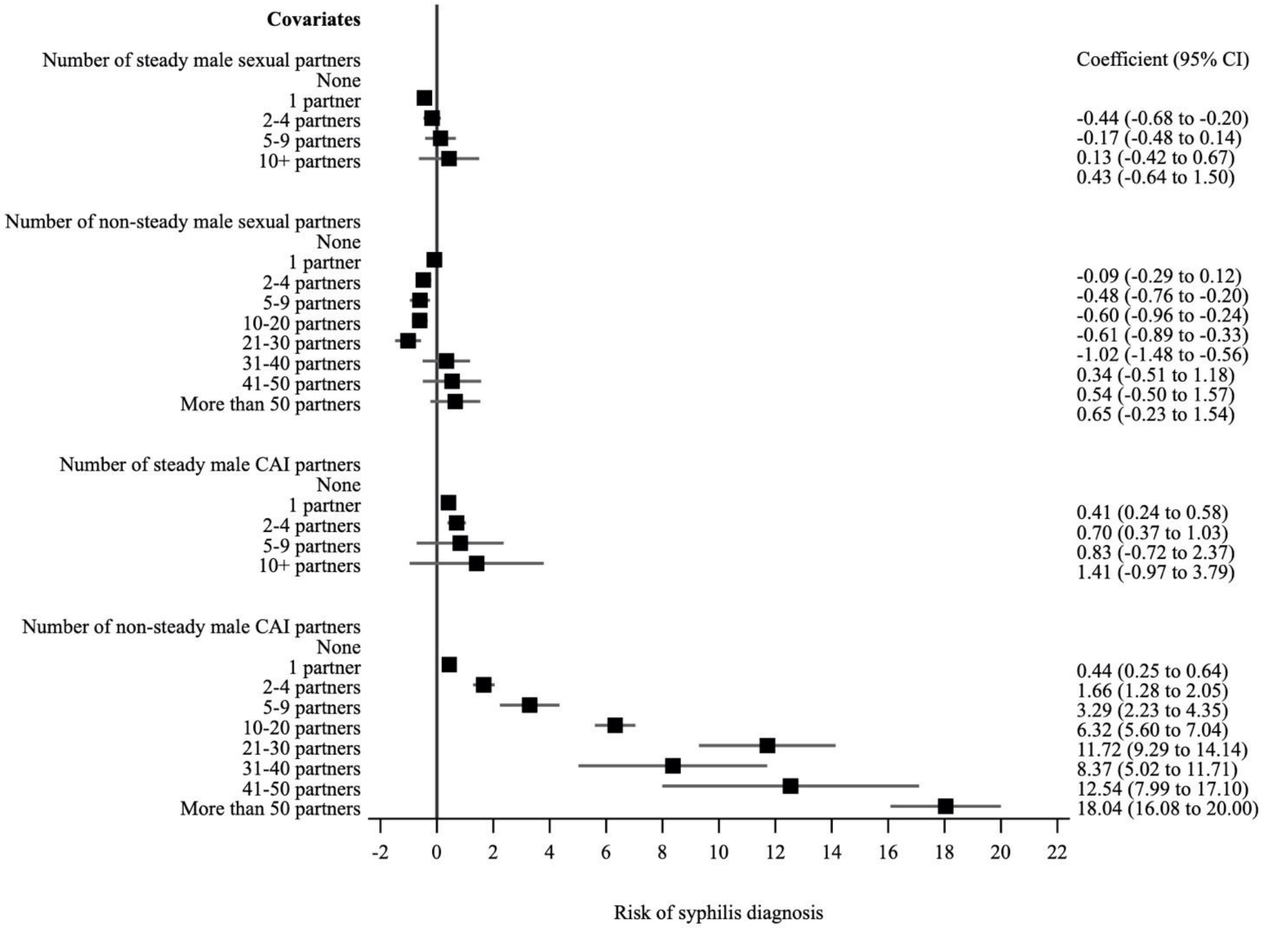
1. Weatherburn P, Schmidt AJ, Hickson F, et al. The European Men-Who-Have-Sex-With-Men Internet Survey (EMIS): Design and Methods. *Sexuality Research and Social Policy* 2013; 10(4): 243-57.
2. Weatherburn P, Hickson F, Reid DS, Marcus U, Schmidt AJ. European Men-Who-Have-Sex-With-Men Internet Survey (EMIS-2017): Design and Methods. *Sexuality Research and Social Policy* 2019.
3. Mendez-Lopez A, Hickson F, Jansen K, et al. What is the empirical basis for converting banded ordinal data on numbers of sex partners among MSM into a continuous scale level variable? A secondary analysis of 13 surveys across 17 countries. *BMC Med Res Methodol* 2022; 22(1): 59.

Appendix 2. Determinants of change in the probability of reporting a syphilis diagnosis within the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017

	Model 1 **Probability of syphilis diagnosis**		**Model 2** **Probability of syphilis diagnosis**	
	Adjusted beta coefficient	95% Confidence Interval	Adjusted beta coefficient	95% Confidence Interval
Year				
2010	reference		reference	
2017	0.0137***	0.0112 to 0.0162	0.0027	-0.0003 to 0.0056
Questionnaire language				
Other than French	reference		reference	
French	0.0763***	0.0538 to 0.0988	0.0671***	0.0495 to 0.0847
Age			0.0008***	0.0005 to 0.0011
Age squared			-0.0001***	-0.0001 to -0.0001
Educational level				
Low			reference	
Mid (at least upper secondary; 2–5 years post 16)			-0.0046***	-0.0071 to -0.0021
High (first stage of tertiary or more; 6+ years post 16)			-0.0106***	-0.0143 to -0.0069
Occupational status				
Employed full/part/self			reference	
Unemployed			0.0033**	0.0010 to 0.0055
Student			-0.0050***	-0.0062 to -0.0039
Retired/Long-term sick leave/Other			-0.0048**	-0.0077 to -0.0019
Settlement size				
Small town/village <100,000 inhabitants.			reference	
Medium/big town ≥100,000 inhabitants			-0.0020	-0.0047 to 0.0006
Country of birth				
Born in country of residence			reference	
Born abroad			0.0051**	0.0014 to 0.0089
Diagnosed with HIV				
No			reference	
Yes			0.0647***	0.0592 to 0.0702
Recency of last screening or testing				
No STI-screening previous 12 months			reference	
Last STI-screening during previous month			0.0595***	0.0445 to 0.0746
Last STI-screening 2–6 months ago			0.0306***	0.0198 to 0.0414
Last STI-screening 7–12 months ago			0.0093*	0.0016 to 0.0170
Symptomatic STI test during previous 12 months			0.1661***	0.1370 to 0.1952
Number of steady male sexual partners in the previous 12 months			0.0002	-0.0001 to 0.0004
Number of non-steady male sexual partners in the previous 12 months			0.0002***	0.0001 to 0.0002
Number of steady male CAI partners in the previous 12 months			0.0008*	0.0002 to 0.0015
Number of non-steady male CAI partners in the previous 12 months			0.0015***	0.0013 to 0.0016
Paid for sex in the previous 12 months				
No			reference	
Yes			0.0058**	0.0020 to 0.0097
Sold sex in the previous 12 months				
No			reference	
Yes			0.0127***	0.0058 to 0.0197
Number of individuals	278,256		234,719	
R^2	0.02		0.14	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; robust standard errors adjusted by country; CAI: condomless anal intercourse. *Note*: In this model, the beta coefficient translates directly to the change in percent points (ppt) after converting the probability (in a scale from 0 to 1) to a percentage (in a scale from 0 to 100).

Appendix 3. Change in the probability of reporting a syphilis diagnosis within the previous 12 months by number of steady and non-steady partners, and number of steady and non-steady condomless anal intercourse (CAI) partners, all within the previous 12 months, in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017



Note: Model adjusted for all covariates in Appendix 2, Model 2. Variables for number of steady and non-steady sexual partners and number of condomless steady and non-steady sexual partners are presented here by categories instead of as continuous variables like in Appendix 2.

Appendix 4. Determinants of change in the number of non-steady male CAI partners within the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017

	Number of non-steady male CAI partners	
	Adjusted beta coefficient	95% Confidence Interval
Year		
2010	reference	
2017	1.62^{***}	1.37 to 1.87
Age	0.13^{***}	0.08 to 0.19
Age squared	-0.01^{***}	-0.01 to -0.01
Educational level		
Low	reference	
Mid at least upper secondary; 2–5 years post 16	0.05	-0.17 to 0.27
High first stage of tertiary or more; 6+ years post 16	-0.28^{*}	-0.52 to -0.04
Occupational status		
Employed full/part/self	reference	
Unemployed	0.24	-0.05 to 0.53
Student	-0.33^{*}	-0.58 to -0.07
Retired/Long-term sick leave/Other	-0.02	-0.23 to 0.19
Settlement size		
Small town/village <100,000 inhabitants	reference	
Medium/big town ≥100,000 inhabitants	0.36^{***}	0.19 to 0.52
Country of birth		
Born in country of residence	reference	
Born abroad	0.24	-0.11 to 0.60
Diagnosed with HIV		
No	reference	
Yes	9.58^{***}	8.34 to 10.81
Recency of last STI-screening or testing		
No STI-screening previous 12 months	reference	
Last STI-screening during previous month	4.29^{***}	3.38 to 5.20
Last STI-screening 2–6 months ago	1.39^{***}	1.13 to 1.64
Last STI-screening 7–12 months ago	-0.25	-0.55 to 0.04
Symptomatic STI test during previous 12 months	4.41^{***}	3.69 to 5.13
Paid for sex in the previous 12 months		
No	reference	
Yes	0.96^{***}	0.63 to 1.29
Sold sex in the previous 12 months		
No	reference	
Yes	6.18^{***}	4.97 to 7.39
Knowledge about HIV undetectable equals untransmissible (U=U)		
I didn't know/understand/believe/wasn't sure	reference	
I knew this already	1.24^{***}	1.04 to 1.45
Serosorting in the previous 12 months*		
No	reference	
Yes	-0.17	-0.61 to 0.28
Number of individuals	203,467	
R^2	0.11	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; robust standard errors adjusted by country; CAI: condomless anal intercourse. * Non-steady male CAI partners based on HIV-serosorting in the previous 12 months.

Appendix 5. Association of PrEP use (currently using PrEP daily or on demand vs not currently using PrEP) with number of non-steady male CAI partners within the previous 12 months, and probability of syphilis diagnosis, in 30 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2017

		Association of PrEP use with the number of non-steady CAI partners and probability of syphilis diagnosis		
		Adjusting for sociodemographic and behavioural variables[a] (except STI-screening)	Adjusting for sociodemographic and behavioural variables[a] (including STI-screening)	Adjusting for sociodemographic and behavioural variables[a] (including STI-screening and number of non-steady CAI partners)
Number of non-steady male CAI partners in the previous 12 months	Not currently taking PrEP	reference	reference	
	PrEP daily or on demand	17.51*** (16.11 to 18.90) *N=77,203*	16.53*** (15.27 to 17.78) *N=74,309*	N/A
Probability of syphilis diagnosis in the previous 12 months [b]	Not currently taking PrEP	reference	reference	reference
	PrEP daily or on demand	0.0861*** (0.0615 to 0.1107) *N=79,416*	0.0530*** (0.0403 to 0.0657) *N=76,535*	0.0285*** (0.0168 to 0.0403) *N=73,456*

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; 95% confidence intervals in brackets; robust standard errors adjusted by country; CAI: condomless anal intercourse.

Note: sample size includes only responses for 2017 and eligible PrEP users (*i.e.*, HIV-diagnosed respondents are excluded from the sample); sample includes only 30 countries as in one country (Latvia) there were no PrEP users.

([a]) models adjusted for all covariates shown in Table 2;

([b]) models adjusted for language of questionnaire.

Appendix 6. Determinants of change in the probability of syphilis diagnosis in the previous 12 months in 31 European countries, European Men-who-have-sex-with-men Internet Survey: EMIS-2010 and EMIS-2017: Testing discrepant cases

	Including all cases	Excluding discrepant cases	Only discrepant cases
Year			
2010	reference	reference	reference
2017	0.0137^{***}	0.0127^{***}	0.0242^{***}
	(0.0112 to 0.0162)	(0.0102 to 0.0152)	(0.0153 to 0.0331)
Number of individuals	278,256	242,397	35,859
R^2	0.02	0.02	0.02

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; 95% confidence intervals in brackets; robust standard errors adjusted by countries.
Models are adjusted for survey wave, language of questionnaire, and country fixed effects.

Discrepant data:
Discrepancies in data arise if answers to two or more questions are logically inconsistent for any of three key variables: age, steady male partners and non-steady partners, each with seven, five and six possible inconsistencies respectively; if a case had at least one inconsistency in any of these three areas, it was flagged as discrepant (n=35,859, 12.89% of the analytic sample).

Supplemental data Study 3

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A8. Sensitivity analyses: Table A8. Country-level determinants (GDP and prevalence of HIV) of HIV public stigma and testing uptake across 40 low- and middle-income countries, latest available data from 2015-2021 (countries with data for all men and women aged 15-49 years, i.e. excluding countries with data only for women or only for ever-married men and women)

A1. Country survey and sample information

Country	Year	Source	Sample size	Gender of respondents
Angola	2015-2016	DHS	16,161	Women and men
Albania	2017-2018	DHS	12,172	Women and men
Argentina	2019-2020	MICS	11,585	Women
Armenia	2015-2016	DHS	7,789	Women and men
Burundi	2016-2017	DHS	23,070	Women and men
Benin	2017-2018	DHS	13,262	Women and men
Bangladesh	2019	MICS	38,903	Women
Belarus	2019	MICS	7,748	Women and men
Central African Republic	2018-2019	MICS	9,869	Women and men
Cameroon	2018-2019	DHS	19,056	Women and men
Congo, Democratic Republic	2017-2018	MICS	22,864	Women and men
Costa Rica	2018	MICS	7,357	Women
Cuba	2019	MICS	12,281	Women and men
Dominican Republic	2019	MICS	21,846	Women
Algeria	2018-2019	MICS	26,234	Women
Ethiopia	2016	DHS	25,542	Women and men
Fiji	2021	MICS	7,263	Women and men
Georgia	2018	MICS	8,531	Women and men
Ghana	2017-2018	MICS	18,424	Women and men
Guinea	2018	DHS	11,957	Women and men
Gambia, The	2019-2020	DHS	15,627	Women and men
Guinea-Bissau	2018-2019	MICS	11,881	Women and men
Honduras	2019-2020	MICS	24,579	Women and men
Haiti	2016-2017	DHS	17,601	Women and men
Indonesia	2017	DHS	46,956	Women and men
India	2019-2021	DHS	183,650	Women and men
Iraq	2018	MICS	15,071	Women
Jordan	2017-2018	DHS	19,190	Women and men
Kyrgyz Republic	2018	MICS	5,560	Women
Kiribati	2018-2019	MICS	5,955	Women and men
Kosovo	2019-2020	MICS	6,355	Women and men
Lao PDR	2017	MICS	21,044	Women and men
Liberia	2019-2020	DHS	11,251	Women and men
Madagascar	2021	DHS	21,576	Women and men
Maldives	2016-2017	DHS	11,423	Women and men
Mali	2018	DHS	11,803	Women and men
Montenegro	2018	MICS	2,885	Women and men
Mongolia	2018	MICS	11,789	Women and men
Mauritania	2019-2021	DHS	18,164	Women and men
Malawi	2019-2020	MICS	30,992	Women and men
Nigeria	2018	DHS	50,448	Women and men
Nepal	2019	MICS	15,972	Women and men
Pakistan	2017-2018	DHS	7,318	Only ever-married women and men
Philippines	2017	DHS	22,813	Women
Papua New Guinea	2016-2018	DHS	18,901	Women and men
Palestine, State of	2019-2020	MICS	9,895	Women
Rwanda	2019-2020	DHS	20,419	Women and men
Sierra Leone	2019	DHS	20,498	Women and men
Sao Tome and Principe	2019	MICS	4,345	Women and men
Suriname	2018	MICS	9,018	Women and men
Chad	2019	MICS	24,348	Women and men
Togo	2017	MICS	8,616	Women and men
Thailand	2019	MICS	34,675	Women and men
Tajikistan	2017	DHS	6,089	Women
Timor-Leste	2016	DHS	4,693	Women and men
Tonga	2019	MICS	3,037	Women and men
Turkmenistan	2019	MICS	6,095	Women
Tunisia	2018	MICS	10,993	Women and men
Tuvalu	2019-2020	MICS	786	Women and men
Uganda	2016	DHS	23,438	Women and men
Vietnam	2020-2021	MICS	12,842	Women and men
Samoa	2019	MICS	3,794	Women and men
Zambia	2018-2019	DHS	24,361	Women and men
Zimbabwe	2019	MICS	14,181	Women and men

A2. Country-level determinants (GDP and prevalence of HIV) of HIV public stigma and testing uptake across 48 low- and middle-income countries, latest available data from 2015-2021 (full results)

	HIV stigma		Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
HIV stigma						
No stigma/Don't know			reference		reference	
Yes stigma			0.66***	0.58 to 0.75	0.74***	0.66 to 0.83
GDP per capita 2017 intl. dollars (PPP) (in thousands)	0.93***	0.91 to 0.95	1.03*	1.00 to 1.05	0.97***	0.95 to 0.98
HIV prevalence	0.85**	0.77 to 0.94	1.71***	1.30 to 2.26	1.37***	1.24 to 1.51
Gender						
Woman	reference		reference		reference	
Man	0.84	0.64 to 1.09	0.40***	0.28 to 0.56	0.62***	0.47 to 0.81
Geographical location						
Urban	reference		reference		reference	
Rural	0.92	0.83 to 1.01	0.73***	0.68 to 0.78	0.73***	0.66 to 0.81
Educational level						
None or pre-primary	reference		reference		reference	
Primary	0.77*	0.63 to 0.94	1.43*	1.08 to 1.90	1.11	0.91 to 1.36
Secondary	0.76	0.57 to 1.01	1.64*	1.07 to 2.50	1.12	0.84 to 1.49
Higher	0.50***	0.38 to 0.67	1.22	0.82 to 1.83	1.14	0.86 to 1.51
Wealth quintile						
Poorest	reference		reference		reference	
Second	0.89***	0.85 to 0.92	0.87	0.74 to 1.03	0.92	0.83 to 1.03
Middle	0.74***	0.70 to 0.79	0.83	0.64 to 1.08	0.89	0.71 to 1.10
Fourth	0.61***	0.54 to 0.70	0.72	0.46 to 1.13	0.91	0.72 to 1.14
Richest	0.53***	0.48 to 0.58	0.82	0.52 to 1.29	0.82	0.55 to 1.23
Age group						
15-19	reference		reference		reference	
20-29	0.89***	0.83 to 0.94	9.14***	5.86 to 14.23	3.40***	2.79 to 4.14
30-39	0.76***	0.70 to 0.83	18.18***	8.39 to 39.39	3.03***	2.39 to 3.82
40-49	0.71***	0.59 to 0.86	10.47***	5.80 to 18.92	1.55***	1.42 to 1.70
Knowledge HIV						
No comprehensive knowledge	reference		reference		reference	
Comprehensive knowledge	0.31***	0.27 to 0.36	1.48***	1.30 to 1.68	1.13	0.92 to 1.39
Number of individuals	1,020,724		884,101		883,767	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; robust standards errors clustered by country; aOR: adjusted odds ratio; CI: confidence interval.

A3. Sensitivity analyses: Table A3. Sociodemographic characteristics and HIV knowledge as drivers of HIV public stigma across 51 low- and middle-income countries, latest available data from 2015-2021 (countries with response rate >70%)

	HIV stigma	
	aOR	95% CI
Gender		
Woman	reference	
Man	0.90^{***}	0.88 to 0.91
Geographical location		
Urban	reference	
Rural	1.02	0.92 to 1.13
Educational level		
None or pre-primary	reference	
Primary	0.72^{***}	0.66 to 0.78
Secondary	0.61^{***}	0.54 to 0.70
Higher	0.41^{***}	0.35 to 0.49
Wealth quintile		
Poorest	reference	
Second	0.90	0.78 to 1.03
Middle	0.75^{***}	0.65 to 0.86
Fourth	0.62^{***}	0.53 to 0.72
Richest	0.54^{***}	0.45 to 0.65
Age group		
15-19	reference	
20-29	0.87^{*}	0.77 to 0.99
30-39	0.71^{***}	0.62 to 0.81
40-49	0.64^{***}	0.56 to 0.74
Knowledge HIV		
No comprehensive knowledge	reference	
Comprehensive knowledge	0.34^{***}	0.30 to 0.38
Number of individuals	968,623	
Number of countries	51	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; model adjusted by country and year indicator variables; robust standards errors; aOR: adjusted odds ratio; CI: confidence interval.

A4. Sensitivity analyses: Table A4. HIV public stigma, HIV knowledge, and sociodemographic drivers of testing uptake across 47 low- and middle-income countries, latest available data from 2015-2021 (countries with response rate >70%)

	Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	95% CI
HIV stigma				
No stigma/Don't know	reference		reference	
Yes stigma	0.68***	0.60 to 0.76	0.77***	0.68 to 0.88
Gender				
Woman	reference		reference	
Man	0.38***	0.37 to 0.39	0.62***	0.60 to 0.63
Geographical location				
Urban	reference		reference	
Rural	0.72***	0.65 to 0.81	0.75***	0.65 to 0.86
Educational level				
None or pre-primary	reference		reference	
Primary	1.99***	1.78 to 2.23	1.54***	1.35 to 1.76
Secondary	2.40***	2.04 to 2.84	1.71***	1.39 to 2.10
Higher	1.86***	1.51 to 2.29	1.78***	1.37 to 2.32
Wealth quintile				
Poorest	reference		reference	
Second	0.86	0.74 to 1.00	0.91	0.75 to 1.12
Middle	0.82*	0.69 to 0.96	0.87	0.72 to 1.05
Fourth	0.70***	0.58 to 0.83	0.88	0.71 to 1.09
Richest	0.79*	0.64 to 0.97	0.77*	0.59 to 0.99
Age group				
15-19	reference		reference	
20-29	10.08***	8.55 to 11.88	3.61***	3.06 to 4.25
30-39	22.27***	18.71 to 26.49	3.31***	2.79 to 3.92
40-49	12.38***	10.35 to 14.80	1.71***	1.40 to 2.09
Knowledge HIV				
No comprehensive knowledge	reference		reference	
Comprehensive knowledge	1.34***	1.16 to 1.55	1.01	0.86 to 1.19
Number of individuals	854,489		854,130	
Number of countries	47		47	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; model adjusted by country and year indicator variables; robust standards errors; aOR: adjusted odds ratio; CI: confidence interval.

A5. Sensitivity analyses: Table A5. Country-level determinants (GDP and prevalence of HIV) of HIV public stigma and testing uptake across 42 low- and middle-income countries, latest available data from 2015-2021 (countries with response rate >70%)

	HIV stigma		Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
HIV stigma						
No stigma/Don't know			reference		reference	
Yes stigma			0.65***	0.57 to 0.74	0.74***	0.66 to 0.83
GDP per capita 2017 intl. dollars (PPP) (in thousands)	0.93***	0.91 to 0.95	1.03	1.00 to 1.05	0.97***	0.95 to 0.98
HIV prevalence	0.85**	0.76 to 0.95	1.69***	1.29 to 2.22	1.36***	1.24 to 1.50
Number of individuals	912,841		814,916		814,586	
Number of countries	42		40		40	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; robust standards errors clustered by country; aOR: adjusted odds ratio; CI: confidence interval.

Note: all models are adjusted for gender, geographical location, educational level, wealth quintile, age group, and knowledge of HIV.

A6. Sensitivity analyses: Table A6. Sociodemographic characteristics and HIV knowledge as drivers of HIV public stigma across 47 low- and middle-income countries, latest available data from 2015-2021 (countries with data for all men and women aged 15-49 years, i.e. excluding countries with data only for women or only for ever-married men and women)

	HIV stigma	
	aOR	95% CI
Gender		
Woman	reference	
Man	0.91^{***}	0.89 to 0.92
Geographical location		
Urban	reference	
Rural	1.11^{***}	1.09 to 1.12
Educational level		
None or pre-primary	reference	
Primary	0.70^{***}	0.69 to 0.71
Secondary	0.55^{***}	0.53 to 0.56
Higher	0.43^{***}	0.41 to 0.44
Wealth quintile		
Poorest	reference	
Second	0.88^{***}	0.86 to 0.90
Middle	0.79^{***}	0.78 to 0.81
Fourth	0.71^{***}	0.69 to 0.72
Richest	0.59^{***}	0.57 to 0.60
Age group		
15-19	reference	
20-29	0.82^{***}	0.80 to 0.83
30-39	0.71^{***}	0.69 to 0.72
40-49	0.72^{***}	0.70 to 0.73
Knowledge HIV		
No comprehensive knowledge	reference	
Comprehensive knowledge	0.36^{***}	0.36 to 0.37
Number of individuals	926,449	
Number of countries	47	

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$; constant calculated but not shown; model adjusted by country and year indicator variables; robust standards errors; aOR: adjusted odds ratio; CI: confidence interval.

A7. Sensitivity analyses: Table A7. HIV public stigma, HIV knowledge, and sociodemographic drivers of testing uptake across 44 low- and middle-income countries, latest available data from 2015-2021 (countries with data for all men and women aged 15-49 years, i.e. excluding countries with data only for women or only for ever-married men and women)

	Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	95% CI
HIV stigma				
No stigma/Don't know	reference		reference	
Yes stigma	0.68^{***}	0.67 to 0.69	0.78^{***}	0.77 to 0.80
Gender				
Woman	reference		reference	
Man	0.39^{***}	0.38 to 0.40	0.60^{***}	0.59 to 0.62
Geographical location				
Urban	reference		reference	
Rural	0.83^{***}	0.81 to 0.85	0.86^{***}	0.84 to 0.88
Educational level				
None or pre-primary	reference		reference	
Primary	1.55^{***}	1.52 to 1.59	1.37^{***}	1.34 to 1.40
Secondary	1.84^{***}	1.78 to 1.90	1.61^{***}	1.56 to 1.67
Higher	1.98^{***}	1.91 to 2.05	1.97^{***}	1.90 to 2.05
Wealth quintile				
Poorest	reference		reference	
Second	1.19^{***}	1.16 to 1.22	1.09^{***}	1.06 to 1.12
Middle	1.38^{***}	1.35 to 1.42	1.19^{***}	1.16 to 1.23
Fourth	1.55^{***}	1.51 to 1.60	1.27^{***}	1.23 to 1.31
Richest	1.74^{***}	1.69 to 1.80	1.29^{***}	1.25 to 1.34
Age group				
15-19	reference		reference	
20-29	6.88^{***}	6.70 to 7.07	3.09^{***}	3.01 to 3.17
30-39	10.46^{***}	10.17 to 10.75	2.83^{***}	2.75 to 2.91
40-49	7.50^{***}	7.28 to 7.73	1.87^{***}	1.81 to 1.93
Knowledge HIV				
No comprehensive knowledge	reference		reference	
Comprehensive knowledge	1.33^{***}	1.30 to 1.36	1.14^{***}	1.12 to 1.17
Number of individuals	822,319		822,042	
Number of countries	44		44	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; model adjusted by country and year indicator variables; robust standards errors; aOR: adjusted odds ratio; CI: confidence interval.

A8. Sensitivity analyses: Table A8. Country-level determinants (GDP and prevalence of HIV) of HIV public stigma and testing uptake across 40 low- and middle-income countries, latest available data from 2015-2021 (countries with data for all men and women aged 15-49 years, i.e. excluding countries with data only for women or only for ever-married men and women)

	HIV stigma		Ever tested for HIV		Tested for HIV past year	
	aOR	95% CI	aOR	aOR	95% CI	aOR
HIV stigma						
No stigma/Don't know			reference		reference	
Yes stigma			0.69^{**}	0.54 to 0.88	0.75^{**}	0.62 to 0.91
GDP per capita 2017 intl. dollars (PPP) (in thousands)	1.00	0.95 to 1.05	1.00	0.95 to 1.04	0.96	0.91 to 1.02
HIV prevalence	0.89^{*}	0.81 to 0.97	1.57^{***}	1.26 to 1.96	1.35^{***}	1.23 to 1.48
Number of individuals	886,547		788,787		788,538	
Number of countries	40		38		38	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; constant calculated but not shown; robust standards errors clustered by country; aOR: adjusted odds ratio; CI: confidence interval.

Note: all models are adjusted for gender, geographical location, educational level, wealth quintile, age group, and knowledge of HIV.

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Table A1 – Latest antiretroviral therapy initiation guidelines by country and year of adoption for countries with test-and-treat (as of August 2017)

Country	Region	CD4 cell count treatment threshold			Year adoption test-and-treat
		Initiation regardless of CD4 count	Initiation at CD4 ≤500	Initiation at CD4 ≤350	
Albania	Eastern Europe & Central Asia		x		
Armenia	Eastern Europe & Central Asia		x		
Austria	EU/EEA	x			2014
Azerbaijan	Eastern Europe & Central Asia			x	
Belgium	EU/EEA		x		
Bulgaria	EU/EEA		x		
Croatia	EU/EEA	x			2015
Denmark	EU/EEA	x			2011
Estonia	EU/EEA	x			2016
France	EU/EEA	x			2013
Georgia	Eastern Europe & Central Asia	x			2015
Germany	EU/EEA	x			2015
Greece	EU/EEA	x			2016
Hungary	EU/EEA	x			2016
Ireland	EU/EEA	x			2017
Israel	Eastern Europe & Central Asia		x		
Italy	EU/EEA	x			2011
Kazakhstan	Eastern Europe & Central Asia		x		
Kyrgyzstan	Eastern Europe & Central Asia		x		
Lithuania	EU/EEA			x	
Luxembourg	EU/EEA		x		
Malta	EU/EEA	x			2016
Moldova	Eastern Europe & Central Asia		x		
Montenegro	Eastern Europe & Central Asia	x			
Netherlands	EU/EEA	x			2012
Poland	EU/EEA	x			2016
Portugal	EU/EEA	x			2016
Romania	EU/EEA	x			2013
Serbia	Eastern Europe & Central Asia	x			2017
Slovenia	EU/EEA	x			2016
Spain	EU/EEA	x			2014
Sweden	EU/EEA	x			2014
Switzerland	EU/EEA	x			2015
Tajikistan	Eastern Europe & Central Asia			x	
Ukraine	Eastern Europe & Central Asia		x		
United Kingdom	EU/EEA	x			2015
Uzbekistan	Eastern Europe & Central Asia		x		

Table A2 – List of countries, region, year of data availability, and antiretroviral therapy policy in the year of data availability

Country	Region	CD4 cell count treatment threshold			Year of available data
		Initiation regardless of CD4 count	Initiation at CD4 ≤500	Initiation at CD4 ≤350	
Albania	Eastern Europe & Central Asia			X	2015
Armenia	Eastern Europe & Central Asia		X		2015
Austria	EU/EEA			X	2013
Azerbaijan	Eastern Europe & Central Asia			X	2015
Belgium	EU/EEA		X		2014
Bulgaria	EU/EEA		X		2015
Croatia	EU/EEA	X			2015
Denmark	EU/EEA	X			2014
Estonia	EU/EEA	X			2015
France	EU/EEA	X			2013
Georgia	Eastern Europe & Central Asia	X			2015
Germany	EU/EEA	X			2015
Greece	EU/EEA			X	2013
Hungary	EU/EEA	X			2015
Ireland	EU/EEA			X	2015
Israel	Eastern Europe & Central Asia		X		2015
Italy	EU/EEA	X			2012
Kazakhstan	Eastern Europe & Central Asia			X	2015
Kyrgyzstan	Eastern Europe & Central Asia		X		2015
Lithuania	EU/EEA			X	2015
Luxembourg	EU/EEA		X		2015
Malta	EU/EEA	X			2016
Moldova	Eastern Europe & Central Asia		X		2015
Montenegro	Eastern Europe & Central Asia	X			2015
Netherlands	EU/EEA	X			2015
Poland	EU/EEA		X		2015
Portugal	EU/EEA		X		2014
Romania	EU/EEA	X			2014
Serbia	Eastern Europe & Central Asia			X	2014
Slovenia	EU/EEA	X			2015
Spain	EU/EEA		X		2013
Sweden	EU/EEA	X			2015
Switzerland	EU/EEA	X			2015
Tajikistan	Eastern Europe & Central Asia			X	2015
Ukraine	Eastern Europe & Central Asia		X		2015
United Kingdom	EU/EEA	X			2015
Uzbekistan	Eastern Europe & Central Asia		X		2015

Table A3 – Summary of ECDC Data sources for the 90-90-90: access to ART and viral suppression

Number of people with HIV that are on ART[1]*:*

Cohort data, 26% of countries (n=8):
Austria, Belgium, Bulgaria, Croatia, Denmark, Luxembourg, Netherlands, Sweden

Surveillance data, 29% of countries (n=9):
Czech Republic, Greece, United Kingdom, Georgia, Kyrgyzstan, Montenegro, Tajikistan, Ukraine, Uzbekistan

Other data source, 45% (n=14):
France, Germany, Ireland, Italy, Malta, Norway, Portugal, Romania, Spain, Azerbaijan, Kazakhstan, Moldova, Serbia, Switzerland

Number of people virally suppressed[1]*:*

Cohort data, 44% of countries (n=12): Austria, Belgium, Bulgaria, Croatia, Denmark, Germany, Greece, Italy, Luxembourg, Netherlands, Sweden, Serbia

Surveillance data, 26% of countries (n=7):
Czech Republic, United Kingdom, Armenia, Georgia, Kyrgyzstan, Montenegro, Tajikistan

Other data source, 30% of countries (n=8):
France, Hungary, Malta, Portugal, Romania, Spain, Azerbaijan, Kazakhstan

References

1. European Centre for Disease Prevention and Control (ECDC). Special report: Continuum of HIV care. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report. Stockholm: European Centre for Disease Prevention and Control; 2017.

Table A4 – Descriptive statistics of countries

	Countries, N	Total number, N (range)
Estimated number of people living with HIV (PLHIV)	37	1,199,107 (194 to 223,000)
People living with HIV diagnosed	37	898,461 (147 to 128,300)
People living with HIV on antiretroviral therapy (ART)	37	698,638 (99 to 114,825)
People living with HIV with viral suppression	30	524,781 (68 to 104,108)
		Mean (range), SD
% of PLHIV diagnosed – 1st 90 UNAIDS target	37	72.8% (38.2 to 98.3), 15.6
% of PLHIV diagnosed on ART – 2nd 90 target	37	70.3% (29.7 to 96.3), 19.9
% of PLHIV diagnosed on ART that have viral suppression – 3rd 90 target	30	77.7% (31.6 to 96.8), 19.1
HIV prevalence	37	0.17% (0.01% to 0.84%), 0.17
GDP per capita in US dollars, purchasing power parity (PPP)	37	\$28,407.4 (\$2,640.3 to \$95,311.1), 18,956.3
Public healthcare expenditures per capita in US dollars, PPP	37	\$1,792.6 (50.5 to 5,463.6), 1,544.1
		Proportion
ART guidelines CD4 cell count threshold		
Initiation at CD4 cell count ≤350	11	29.7%
Initiation at CD4 cell count ≤500	10	27.1%
Initiation regardless of CD4 cell count (test-and-treat)	16	43.2%
Year of available data for the UNAIDS 90-90-90 target		
2012	1	2.7%
2013	4	10.8%
2014	5	13.5%
2015	26	70.3%
2016	1	2.7%
Region		
EU/EEA	24	64.9%
Eastern Europe and Central Asia	13	35.1%

Supplemental data Study 5:

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Figure A1. Prevalence of worsened depression due to the COVID-19 pandemic in 26 European countries, June-August 2020

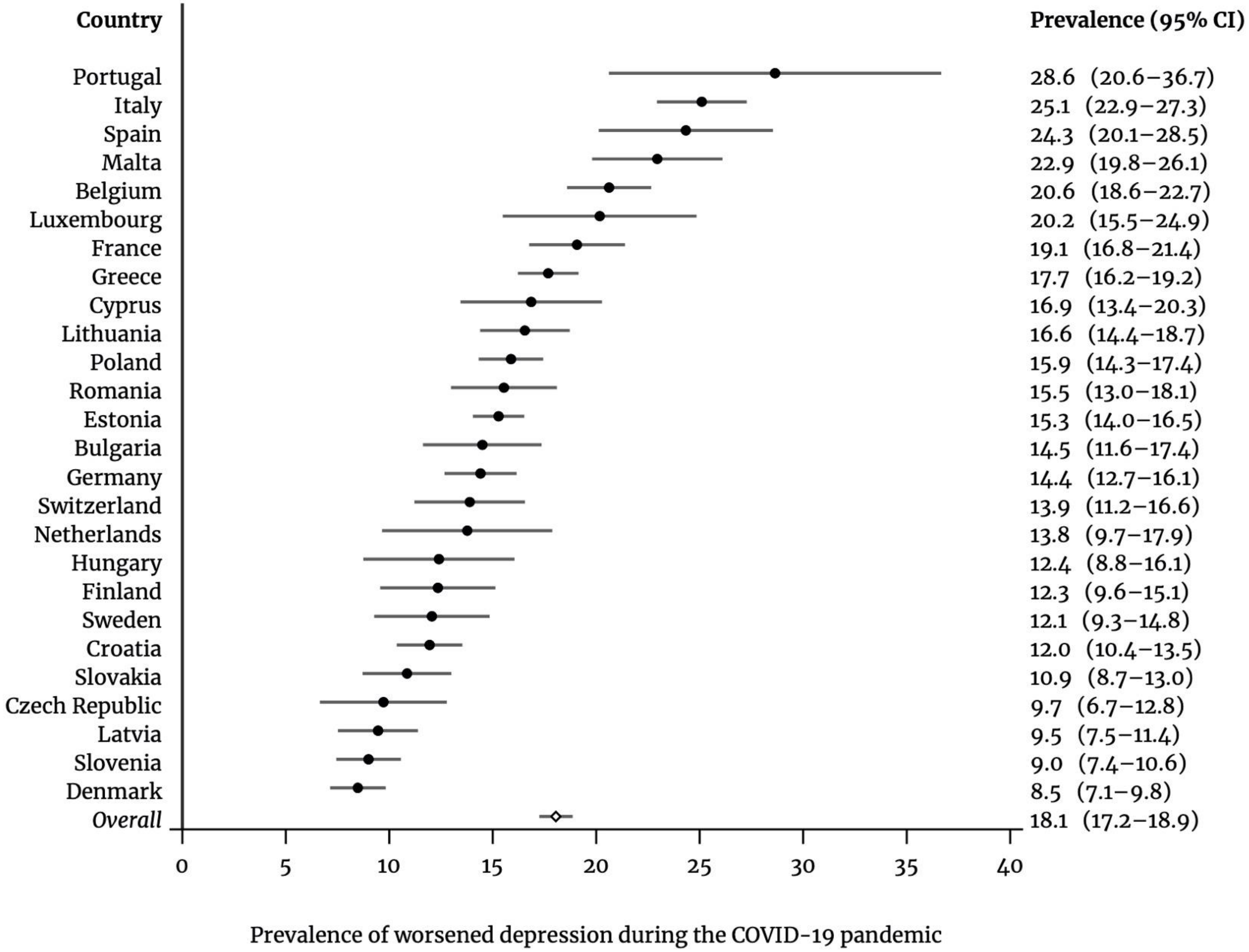

Figure A2. Prevalence of worsened anxiety due to the COVID-19 pandemic in 26 European countries, June-August 2020

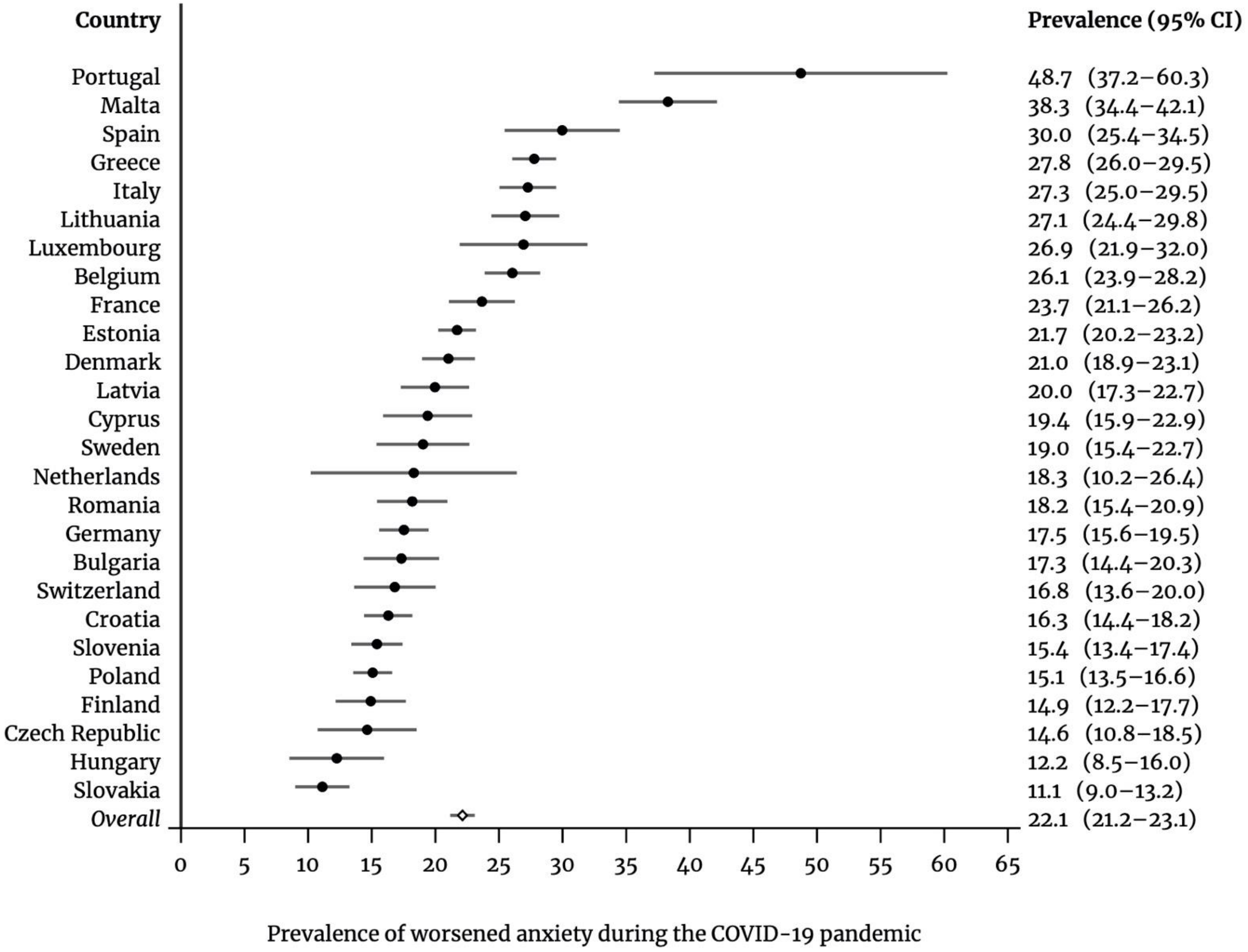

Table A1. Individual-level determinants of change in the probability of worsened depression during the COVID-19 pandemic in 26 European countries, June-August 2020

	Worsened depression during the COVID-19 pandemic
Age group	
50-64	reference
65-79	-0.00593
	(-0.0302–0.0183)
80+	-0.00206
	(-0.0231–0.0190)
Gender	
Male	reference
Female	0.103***
	(0.0731–0.133)
Self-rated health before pandemic	
Excellent	reference
Very good	0.00861
	(-0.0110–0.0282)
Good	0.0331**
	(0.0107–0.0555)
Fair	0.115***
	(0.0802–0.149)
Poor	0.195***
	(0.167–0.223)
Respondent COVID-19 positive	
Not positive	reference
Positive	0.121*
	(0.00572–0.237)
Anyone known COVID-19 positive	
No	reference
Yes	-0.00655
	(-0.0501–0.0370)
Forgone healthcare during pandemic	
No	reference
Yes	0.0993***
	(0.0781–0.120)
Living alone	
2 or more in household	reference
1 person in household (living alone)	0.0228**
	(0.00906–0.0365)
Make ends meet during pandemic	
Easily/Fairly easily	reference
With some/great difficulty	0.0492***
	(0.0302–0.0682)
Working before pandemic	
No or Retired	reference
Yes	-0.0118
	(-0.0420–0.0185)
Became unemployed during pandemic	
No or Retired	reference
Yes	0.0610***
	(0.0315–0.0904)
Number of indivudals	48549
R^2	0.074

95% confidence intervals in brackets.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

Robust standard errors clustered by country; constant calculated but not shown; all models adjusted by country indicator variables.

Table A2. Impact of stringency of policy responses to the pandemic on the change in the probability of worsened depression during the COVID-19 pandemic in 26 European countries, June-August 2020

	Worsened depression during the COVID-19 pandemic	
	Model 1	Models 2-9
Total COVID-19 cases per million inhabitants	0.0000256*** (0.0000188–0.0000325)	
Stringency index of policy responses to the pandemic	0.00190** (0.000660–0.00314)	
Stringency index components:		
C1 School closing		0.0203 (-0.00470–0.0453)
C2 Workplace closing		0.0476* (0.0108–0.0843)
C3 Cancel public events		0.00426 (-0.0351–0.0436)
C4 Restrictions on gathering size		0.00200 (-0.0224–0.0264)
C5 Close public transport		0.0235 (-0.00530–0.0524)
C6 Stay at home requirements		0.0240* (0.00408–0.0439)
C7 Restrictions on internal movement		0.0143 (-0.00198–0.0307)
C8 Restrictions on international travel		-0.00944 (-0.0356–0.0167)
Number of individuals	48549	48549
Number of countries	26	26
R^2	0.074	–

95% confidence intervals in brackets.
$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$
Constant calculated but not shown.
Models 1-9 are adjusted for all variables included in Model 3, Table 2.
Models 2-9 are adjusted for total COVID-19 cases per million inhabitants.
C: component.

Table A3. Impact of social protection expenditures on the change in the probability of worsened depression during the COVID-19 pandemic in 26 European countries, June-August 2020

		Worsened depression during the COVID-19 pandemic
		Models 1-9
	Sample	
Per 1,000 € increase in social protection expenditures per capita	*All* (n=49862)	-0.00532** (-0.00864–-0.00200)
	Poor/fair health (n=16513)	-0.00585 (-0.0119–0.000209)
	Unemployed (n=1888)	-0.0165* (-0.0318–-0.00121)
	≥65 years old (n=35283)	-0.00439** (-0.00723–-0.00154)
	Difficulty make ends meet (n=17416)	0.00219 (-0.00595–0.0103)
Per 1,000 € increase in health care/sickness expenditures per capita		
	All (n=49862)	-0.0160*** (-0.0237–-0.00830)
	Poor/fair health (n=16513)	-0.0184* (-0.0335–-0.00340)
Per 1,000 € increase in unemployment benefits expenditures per capita		
	Unemployed (n=1888)	-0.139 (-0.447–0.168)
Per 1,000 € increase in pensions/old age expenditures per capita	*≥65 years old* (n=35283)	0.0000348 (-0.00849–0.00856)

95% confidence intervals in brackets.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

Constant calculated but not shown.

All models adjusted by age, gender, health status before the pandemic, tested positive for COVID-19 oneself or someone close, household size, total COVID-19 cases per million inhabitants, and stringency index of policy responses to the pandemic.

Table A4. Individual-level determinants of change in the probability of worsened anxiety during the COVID-19 pandemic in 26 European countries, June-August 2020

	Worsened anxiety during the COVID-19 pandemic
Age group	
50-64	reference
65-79	-0.0282^{*}
	(-0.0548,-0.00165)
80+	-0.0570^{***}
	(-0.0718,-0.0423)
Gender	
Male	reference
Female	0.0944^{***}
	(0.0643,0.124)
Self-rated health before pandemic	
Excellent	reference
Very good	0.0254
	(-0.00133,0.0521)
Good	0.0692^{***}
	(0.0342,0.104)
Fair	0.144^{***}
	(0.114,0.174)
Poor	0.201^{***}
	(0.157,0.244)
Respondent COVID-19 positive	
Not positive	reference
Positive	0.0670
	(-0.0456,0.179)
Anyone known COVID-19 positive	
No	reference
Yes	0.0296
	(-0.0161,0.0754)
Forgone healthcare during pandemic	
No	reference
Yes	0.128^{***}
	(0.0905,0.165)
Living alone	
2 or more in household	reference
1 person in household (living alone)	0.000318
	(-0.0168,0.0175)
Make ends meet during pandemic	
Easily/Fairly easily	reference
With some/great difficulty	0.0495^{***}
	(0.0339,0.0651)
Working before pandemic	
No or Retired	reference
Yes	-0.00499
	(-0.0180,0.00802)
Became unemployed during pandemic	
No or Retired	reference
Yes	0.0725^{*}
	(0.0157,0.129)
Number of individuals	48560
R^2	0.074

95% confidence intervals in brackets.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

Robust standard errors clustered by country; constant calculated but not shown; all models adjusted by country indicator variables.

Table A5. Impact of stringency of policy responses to the pandemic on the change in the probability of worsened anxiety during the COVID-19 pandemic in 26 European countries, June-August 2020

	Worsened anxiety during the COVID-19 pandemic	
	Model 1	Models 2-9
Total COVID-19 cases per million inhabitants	0.0000314*** (0.0000239–0.0000390)	
Stringency index of policy responses to the pandemic	0.000975 (-0.000396–0.00235)	
Stringency index components:		
C1 School closing		-0.0189 (-0.0471–0.00925)
C2 Workplace closing		0.0183 (-0.0231–0.0598)
C3 Cancel public events		-0.00549 (-0.0528–0.0418)
C4 Restrictions on gathering size		0.0370* (0.00817–0.0659)
C5 Close public transport		0.0450* (0.00522–0.0848)
C6 Stay at home requirements		0.0306* (0.00653–0.0547)
C7 Restrictions on internal movement		-0.00585 (-0.0277–0.0160)
C8 Restrictions on international travel		-0.0579*** (-0.0897–-0.0260)
Number of individuals	48560	48560
Number of countries	26	26
R^2	0.068	–

95% confidence intervals in brackets.
$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$
Constant calculated but not shown.
Models 1-9 are adjusted for all variables included in Model 3, Table 2.
Models 2-9 are adjusted for total COVID-19 cases per million inhabitants.
C: component.

Table A6. Impact of social protection expenditures on the change in the probability of worsened anxiety during the COVID-19 pandemic in 26 European countries, June-August 2020

		Worsened anxiety during the COVID-19 pandemic
		Models 1-9
	Sample	
Per 1,000 € increase in social protection expenditures per capita	*All* (n=49871)	-0.00527* (-0.00932–-0.00121)
	Poor/fair health (n=16516)	-0.0127*** (-0.0201–-0.00528)
	Unemployed (n=1888)	-0.0244** (-0.0415–-0.00726)
	≥65 years old (n=35286)	-0.00713*** (-0.0101–-0.00413)
	Difficulty make ends meet (n=17421)	-0.00238 (-0.0118–0.00707)
Per 1,000 € increase in health care/sickness expenditures per capita		
	All (n=49871)	-0.0161*** (-0.0255–-0.00665)
	Poor/fair health (n=16516)	-0.0305*** (-0.0483–-0.0127)
Per 1,000 € increase in unemployment benefits expenditures per capita		
	Unemployed (n=1888)	-0.414* (-0.742–-0.0857)
Per 1,000 € increase in pensions/old age expenditures per capita	*≥65 years old* (n=35286)	-0.00820 (-0.0173–0.000897)

95% confidence intervals in brackets.
$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$
Constant calculated but not shown.
All models adjusted by age, gender, health status before the pandemic, tested positive for COVID-19 oneself or someone close, household size, total COVID-19 cases per million inhabitants, and stringency index of policy responses to the pandemic.