The impact of regional socioeconomic deprivation on late HIV diagnoses: a cross-sectional study in Germany

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Abstract

Background: Late HIV diagnoses are associated with significantly poorer health outcomes and facilitate onward transmission. The proportion of HIV infections diagnosed at advanced stages has remained continuously high in Germany. This study examined the effect of regional socioeconomic deprivation on late HIV presentation.

Methods: We used data from the national statutory notification of newly diagnosed HIV cases collected between 2011 and 2018 with further information on the timing of diagnosis determined by the BED-Capture-ELISA test (BED-CEIA) and diagnosing physicians. Data on regional socioeconomic deprivation were derived from the German Index of Socioeconomic Deprivation (GISD). Outcome measures were a long-standing infection based on the BED-CEIA result or an infection at the stage of AIDS. The effect of socioeconomic deprivation on the timing of diagnosis was analysed using multivariable Poisson regression models with cluster-robust error variance.

Results: Overall, 66.2% (n=6,185) of the patients were diagnosed with a long-standing infection and 13.1% (n=1,536) with AIDS. The proportion of late diagnoses was higher among persons with heterosexual contact compared to men who have sex with men (MSM) (76.5% long-standing and 16.4% AIDS vs. 62.4% long-standing and 11.9% AIDS). MSM living in highly deprived countryside regions were more likely to have a long-standing infection (aPR: 1.16, 95% CI 1.05-1.28) as well as AIDS (aPR: 1.41, 95% CI 1.08-1.85) at the time of diagnosis compared to MSM in less deprived countryside regions. No differences were observed among MSM from urban areas, and no differences overall among persons with heterosexual contact.

Conclusions: An effect of socioeconomic deprivation on late HIV presentation was found only in MSM from countryside regions. We suggest that efforts in promoting HIV awareness and regular HIV testing are increased for heterosexual persons irrespective of socioeconomic background, and for MSM with a focus on persons living in deprived regions in the countryside.

Background

The time between an HIV infection and its diagnosis can vary widely across individuals. An undiagnosed and/or untreated infection advances with a progressive depletion of CD4 cells and a continuous decrease in immune functioning [1]. This progression can be prevented by antiretroviral therapy (ART) in most patients [2]. Late HIV diagnoses and a delayed commencement of ART therefore pose severe health risks to the individual and are also concerning on the population health level.

Persons with a deferred start of ART have a greater decline of CD4 cells and a significantly increased risk of developing AIDS-defining illnesses compared to people with an early start of ART [3]. Late presentation is also associated with substantially higher medical health care costs resulting from increased treatment needs of patients with advanced HIV infections [4, 5]. On the population health level, late diagnoses are concerning as they facilitate further transmission through individuals who are unaware of their status [6].

Early diagnosis and treatment furthermore play a pivotal role in controlling HIV transmission in populations as effective ART leads to viral suppression and the practical elimination of a risk for onward sexual transmission [7]. In this regard, UNAIDS had set the 90-90-90 targets that were extended to the 95-95-95 targets, aiming to have diagnosed 95% of all HIV positive people, provided ART for 95% of all those diagnosed and achieved viral suppression for 95% of those treated by 2030 [8].

Despite continuous efforts with respect to awareness campaigns and an increased focus on testing [9], in Europe an estimated 40-60% of persons is diagnosed with a CD4 cell count below 350 cells/mm³ and/or has experienced an AIDS-defining illness at the time of diagnosis [10]. The highest proportions are found in the age groups of 50 years and older and among people who acquired HIV via heterosexual contact [10, 11]. A similar distribution can be observed in Germany [12]. In 2019, around half of the HIV infections were diagnosed at later stages with 34% at the stage of advanced immunodeficiency and 15% with AIDS. These numbers have remained continuously high since the early 2000s. Here, the highest proportions of late diagnoses were also found among the older age groups, persons with heterosexual contact as well as migrants from Sub-Saharan Africa and Asia and the Pacific [12, 13].

In order to reduce the number of late HIV diagnoses, it is necessary to gain a better understanding of the underlying factors that play a role in HIV health behaviours. Socioeconomic status (SES) is a factor whose impact on health has been widely investigated. Whether measured by poverty, education, social class or other indicators, low SES predicts worse health for a wide range of health behaviours and outcomes [14]. For HIV and AIDS, some studies underline this link, showing that individuals of lower SES are at a disproportionately higher risk for contracting HIV, presenting at later stages and also have higher mortality rates [15–17]. In Germany, this relationship has not been examined yet. As the HIV surveillance system does not include information on socioeconomic factors at the individual patient level, this study utilised the German Index of Socioeconomic Deprivation (GISD), which describes socioeconomic inequalities at different regional levels in Germany [18]. The GISD was generated at the levels of associations of municipalities, administrative districts and administrative regions and is based on the sub-dimensions of education, occupation, and income. The calculated deprivation scores depict the socio-spatial burden in the respective area and can be utilised to investigate the link between regional socioeconomic deprivation and health.

Using the GISD, this study aimed to examine whether socioeconomic deprivation in Germany affects the timing of HIV diagnosis. Knowledge about its potential impact on late HIV presentation can be used to improve and render public health strategies aimed at promoting HIV awareness and early testing behaviours more effectively.

Methods

Study design

This study is a cross-sectional study using data from the “InzSurv-HIV” study at the Robert Koch Institute (RKI) in Germany. The dataset contains pseudonymised information from the national statutory notification of newly diagnosed HIV cases that are directly reported to the RKI. For about 60% of the new diagnoses, the RKI additionally receives dried serum or plasma spots from participating laboratories which are then tested for recency of infection using the BED-Capture-ELISA (BED-CEIA) [19, 20]. Cases are classified as recent or long-standing with a cut-off point that corresponds to a mean duration of approximately five months after the infection [21]. Since the BED-CEIA might produce false-recent results in people with advanced immunodeficiency, cases classified as recent while diagnosed with an AIDS-defining condition were considered long-standing infections. Included in this analysis were all cases from 2011 to 2018. Excluded were cases with the age below 15 years at the time of diagnosis as well as cases with a transmission mode of blood transfusion, haemophilia, occupational exposition and mother to child transmission due to sparse data. The GISD data were linked to this dataset on the basis of the 3-digit ZIP code with each patient receiving the respective socioeconomic deprivation score of their residential area. In addition to that, data on city population size were derived from the Federal Statistical Office of Germany and merged to the dataset [22].

Outcomes and covariates

The risk for late HIV diagnoses was examined at two time points: The first outcome was an HIV diagnosis at the stage of a long-standing infection as determined by the BED-CEIA assay. A long-standing HIV infection is defined as an infection that has been diagnosed after a mean duration of more than approximately 20 weeks (=5 months) since it was acquired [21]. The second outcome was an HIV infection that was diagnosed at the clinical stage of AIDS. This outcome was derived from the CDC classification system for HIV diagnoses in which category C classifies patients who have already developed an AIDS-defining condition at the time of their HIV diagnosis [23]. The classification was done by the diagnosing physician and reported to the RKI via the statutory notification.

While the first outcome identifies all cases diagnosed after the acute phase, the second outcome is more specific and only looks at diagnoses received at a further advanced stage with an AIDS-defining condition. The two outcome measures depict different points in time with regard to HIV progression and were analysed separately.

The exposure of interest was regional socioeconomic deprivation using the GISD score, which is based on the sub-dimensions of education, occupation, and income [18, 24]. The calculated index values were divided into quintiles and then grouped into three categories, representing low deprivation (lowest quintile), medium deprivation (middle three quintiles) and high deprivation (highest quintile). High socioeconomic deprivation can be equally understood as a lack of socioeconomic resources or low socioeconomic status [18].

Further variables included in the analysis were transmission mode (men who have sex with men (MSM), persons with heterosexual contact (HET), persons who inject drugs (PWID)), sex (male, female), approximated age at the time of infection (15-19, 20-29, 30-39, 40-49, 50-59, 60-69, >69 years), region of

origin (Western and Central Europe, Asia and the Pacific, Caribbean, Eastern Europe and Central Asia, Latin America, Middle East and North Africa, North America, Sub-Saharan Africa) and city size (countryside: <100k residents, town: 100k - <1 million residents, major city: $\geq$ 1 million residents). As the age at the time of infection is unknown, this variable was approximated from the available age at the time of diagnosis by subtracting the approximate median progression periods on the basis of the CDC classification system [23]. We subtracted one age year from cases classified as category A (acute, asymptomatic infection), five age years from cases classified as category B (chronic, symptomatic infection), and ten age years from cases classified as category C (AIDS) [23, 25, 26]. No age years were subtracted from cases younger than 30 years at the time of diagnosis to avoid computing unrealistic outliers in the lower end age groups. Even though the median time periods until the development of AIDS decrease with older age [25], this procedure is justified as persons who are diagnosed with an AIDS-defining illness at a younger age usually have shorter lags between HIV contraction and diagnosis, while persons diagnosed with AIDS in the older age groups tend to have longer lags.

Statistical analysis

Separate complete case analyses were conducted for both outcome measures. To estimate the effect of socioeconomic deprivation on late presentation, prevalence ratios using multivariable Poisson regressions with ZIP code cluster-robust error variance to account for the individual and regional level data structure were computed. The models were adjusted for the variables of transmission mode, sex, approximated age at the time of infection, region of origin and city size. These variables were identified as confounders by a directed acyclic graph, which was created on the basis of prior research (see Figure S1, Additional file 1). Stratified analyses were performed for MSM and persons with heterosexual contact as effect modification was expected for these groups due to their differing health seeking behaviours with respect to HIV [13]. In the case of discernible effects, an interaction term between the GISD and city size was planned to be included in the models to examine a potential interaction of these variables, seeing that HIV support structures in urban areas differ from those in rural areas [27]. Adjusted prevalence ratios (aPR) and 95% confidence intervals (95% CI) were calculated.

Results

After excluding all cases with missing data, a total of 9,342 cases with BED-CEIA results and 11,774 cases with a documented CDC category were included in the analysis. Among the 9,342 patients with available BED-CEIA test results, 66.2% had an HIV infection classified as long-standing at the time of diagnosis (Table 1). Patients in the highest socioeconomic deprivation quintile showed a slightly higher proportion of long-standing infections (68.9%) compared to the low (66.2%) and medium deprivation quintiles (65.8%). With regard to the other variables included in the analysis, the highest proportions of long-standing infections were found in the heterosexual transmission group (76.5%) and among migrants from Sub-Saharan Africa (79.2%). Among the 11,774 patients with a documented CDC category, 13.1% had reached the clinical stage of AIDS at the time of their diagnosis (Table 1). Patients living in regions with the highest socioeconomic deprivation were more often diagnosed with an AIDS-defining condition

(16.2%) than patients of low (12.7%) and medium deprivation (12.7%) background. Concerning the other variables, the highest proportions of AIDS-defining conditions were observed in the heterosexual transmission group (16.4%) and patients between 60 and 69 years at the time of diagnosis (28.2%) (Table 1).

Table 1 Baseline data of newly diagnosed HIV cases by BED-CEIA ¹ recency test and CDC category				
N=11,774	N=9,342			
	Long-standing infection	Recent infection	AIDS	No AIDS
Total	6,185 (66.2%)	3,157 (33.8%)	1,536 (13.1%)	10,238 (86.9%)
GISD ²				
Low deprivation	1,663 (66.2%)	849 (33.8%)	410 (12.7%)	2,812 (87.3%)
Medium deprivation	3,909 (65.8%)	2,031 (34.2%)	929 (12.7%)	6,404 (87.3%)
High deprivation	613 (68.9%)	277 (31.1%)	197 (16.2%)	1,022 (83.8%)
Transmission mode				
MSM ³	4,061 (62.4%)	2,450 (37.6%)	973 (11.9%)	7,225 (88.1%)
HET ⁴	1,905 (76.5%)	586 (23.5%)	509 (16.4%)	2,604 (83.6%)
PWID ⁵	219 (64.4%)	121 (35.6%)	54 (11.7%)	409 (88.3%)
Sex				
Male	4,850 (64.2%)	2,708 (35.8%)	1,215 (12.7%)	8,348 (87.3%)
Female	1,335 (74.8%)	449 (25.2%)	321 (14.5%)	1,890 (85.5%)
Age (time of diagnosis)				
15 to 19	92 (51.7%)	86 (48.3%)	8 (4.4%)	176 (95.6%)
20 to 29	1,512 (60.2%)	1,000 (39.8%)	153 (5.1%)	2,850 (94.9%)
30 to 39	2,034 (66.4%)	1,029 (33.6%)	427 (11.2%)	3,390 (88.8%)
40 to 49	1,534 (70.7%)	636 (29.3%)	490 (17.2%)	2,366 (82.8%)

50 to 59	746 (71.3%)	301 (28.7%)	317 (22.5%)	1,090 (77.5%)
60 to 69	211 (73.3%)	77 (26.7%)	113 (28.2%)	288 (71.8%)
>69	56 (66.7%)	28 (33.3%)	28 (26.4%)	78 (73.6%)
Approx. age (time of infection)				
15 to 19	92 (51.7%)	86 (48.3%)	8 (4.4%)	176 (95.6%)
20 to 29	2,267 (66.5%)	1,143 (33.5%)	580 (14.2%)	3,510 (85.8%)
30 to 39	1,957 (66.6%)	980 (33.4%)	490 (13.1%)	3,245 (86.9%)
40 to 49	1,278 (67.5%)	615 (32.5%)	317 (12.6%)	2,209 (87.4%)
50 to 59	446 (64.3%)	248 (35.7%)	113 (12.0%)	831 (88.0%)
60 to 69	119 (65.0%)	64 (35.0%)	27 (11.2%)	214 (88.8%)
>69	26 (55.3%)	21 (44.7%)	1 (1.9%)	53 (98.1%)
Region of origin				
Western and Central Europe	4,462 (63.2%)	2,600 (36.8%)	1,152 (12.8%)	7,859 (87.2%)
Asia and the Pacific	195 (72.5%)	74 (27.5%)	66 (19.5%)	272 (80.5%)
Caribbean	25 (69.4%)	11 (30.6%)	4 (8.7%)	42 (91.3%)
Eastern Europe and Central Asia	214 (72.1%)	83 (27.9%)	50 (13.3%)	327 (86.7%)
Latin America	119 (66.5%)	60 (33.5%)	20 (8.4%)	219 (91.6%)
Middle East and North Africa	107 (69.9%)	46 (30.1%)	16 (8.5%)	172 (91.5%)
North America	25 (71.4%)	10 (28.6%)	5 (11.1%)	40 (88.9%)
Sub-Saharan Africa	1,038 (79.2%)	273 (20.8%)	223 (14.6%)	1,307 (85.4%)

City size				
Countryside <100k res.	2,651 (69.1%)	1,184 (30.9%)	704 (14.7%)	4,077 (85.3%)
Town 100k - <1 million res.	1,946 (64.5%)	1,071 (35.5%)	456 (12.5%)	3,189 (87.5%)
Major city >= 1 million res.	1,588 (63.8%)	902 (36.2%)	376 (11.2%)	2,972 (88.8%)
¹ <i>BED-CEIA</i> BED-Capture-ELISA recency test, ² <i>GISD</i> German Index of Socioeconomic Deprivation,				
³ <i>MSM</i> Men who have sex with men, ⁴ <i>HET</i> Persons with heterosexual contact, ⁵ <i>PWID</i> Persons who inject drugs				

The results of the stratified multivariable analyses of the BED-CEIA outcome measure showed that MSM living in regions that belong to the highest socioeconomic deprivation quintile were somewhat more likely to have a long-standing infection at the time of diagnosis (aPR: 1.06, 95% CI 0.99-1.13) compared to MSM in regions of lower deprivation (Table 2). In the heterosexual transmission group, no differences between persons of high, medium or low socioeconomic deprivation background were observed (Table 2). An interaction term between the GISD and city size was included in the regression model of the MSM stratum, which showed that these variables interact with each other. While MSM from highly and medium deprived countryside areas were more likely to have a long-standing HIV infection at the time of diagnosis (aPR: 1.16, 95% CI 1.05-1.28; aPR: 1.09, 95% CI 1.01-1.18) compared to MSM from countryside areas of low socioeconomic deprivation (Table 3), no differences in the adjusted prevalence ratios were observed between MSM from towns or major cities with different deprivation levels (Table 3).

The results of the stratified multivariable analyses of the CDC outcome measure showed that MSM living in regions belonging to the highest socioeconomic deprivation quintile were somewhat more likely to have reached the clinical stage of AIDS at the time of diagnosis (aPR: 1.21, 95% CI 0.98-1.50) compared to MSM in regions of lower deprivation (Table 4). In the heterosexual transmission group, again no differences between persons of high, medium or low socioeconomic deprivation background were observed (Table 4). In this analysis, an interaction term between the GISD and city size was also included in the regression model of the MSM stratum, which again revealed an interaction of the same type between these variables. While MSM living in highly deprived countryside areas were more likely to have

Table 2 Multivariable analysis of long-standing HIV infections stratified for transmission mode						
	n=2,491			n=6,511		
		MSM ²			HET ³	
	n (%)†	aPR [95% CI]‡	p-value	n (%)†	aPR [95% CI]‡	p-value
GISD ¹						
Low deprivation	1,052 (61.7%)	1		556 (76.9%)	1	
Medium deprivation	2,611 (62.1%)	1.00 [0.96, 1.05]	0.873	1,161 (76.5%)	1.00 [0.95, 1.05]	0.940
High deprivation	398 (66.0%)	1.06 [0.99, 1.13]	0.091	188 (74.9%)	0.98 [0.90, 1.05]	0.535
Sex						
Male	4,061 (62.4%)	1		618 (78.5%)	1	
Female		(omitted)		1,287 (75.5%)	0.95 [0.91, 1.00]	0.030
Approx. age (time of infection)						
15 to 19	43 (38.1%)	0.60 [0.47, 0.76]	<0.001	49 (76.6%)	1.00 [0.88, 1.15]	0.919
20 to 29	1,485 (61.6%)	0.98 [0.93, 1.02]	0.342	703 (79.3%)	1.04 [0.99, 1.09]	0.129
30 to 39	1,235 (62.8%)	1		632 (76.1%)	1	
40 to 49	935 (66.1%)	1.05 [1.00, 1.10]	0.044	310 (74.9%)	0.99 [0.93, 1.07]	0.854
50 to 59	275 (59.9%)	0.95 [0.88, 1.03]	0.185	156 (73.2%)	0.99 [0.90, 1.08]	0.769
60 to 69	74 (62.7%)	1.00 [0.85, 1.17]	0.987	43 (68.3%)	0.92 [0.78, 1.09]	0.333

>69	14 (50.0%)	0.80 [0.58, 1.11]	0.181	12 (63.2%)	0.86 [0.60, 1.24]	0.416
Region of origin						
Western and Central Europe	3,685 (62.2%)	1		631 (70.8%)	1	
Asia and the Pacific	103 (65.6%)	1.07 [0.96, 1.20]	0.222	89 (81.7%)	1.16 [1.04, 1.28]	0.007
Caribbean	14 (70.0%)	1.14 [0.84, 1.54]	0.407	11 (68.8%)	0.98 [0.70, 1.37]	0.889
Eastern Europe and Central Asia	44 (57.1%)	0.93 [0.77, 1.12]	0.433	109 (77.3%)	1.08 [0.98, 1.20]	0.107
Latin America	105 (66.0%)	1.09 [0.98, 1.20]	0.101	13 (68.4%)	0.97 [0.71, 1.32]	0.838
Middle East and North Africa	49 (62.8%)	1.02 [0.85, 1.23]	0.802	54 (80.6%)	1.11 [0.98, 1.25]	0.089
North America	24 (72.7%)	1.19 [0.92, 1.54]	0.191	1 (50.0%)	0.69 [0.17, 2.90]	0.616
Sub-Saharan Africa	37 (60.7%)	1.01 [0.82, 1.25]	0.911	997 (80.0%)	1.12 [1.06, 1.18]	<0.001
City size						
Countryside <100k res.	1,578 (64.5%)	1.06 [1.00, 1.12]	0.041	971 (77.7%)	1.03 [0.96, 1.11]	0.397
Town 100k - <1 million res.	1,289 (61.0%)	1.00 [0.95, 1.06]	0.988	578 (75.1%)	1.00 [0.92, 1.08]	0.980
Major city >= 1 million res.	1,194 (61.1%)	1		356 (75.6%)	1	

¹ *GISD* German Index of Socioeconomic Deprivation, ² *MSM* Men who have sex with men,

³ *HET* Persons with heterosexual contact

†Strata specific number and proportion of long-standing infections at the time of diagnosis.

‡Prevalence ratios with corresponding 95% confidence intervals of long-standing infections at the time of diagnosis were calculated for the exposure variable *GISD* using stratified multivariable Poisson regression with ZIP code cluster-robust error variance (standard errors were adjusted for 626

clusters in the MSM stratum and 562 clusters in the HET stratum). The models were adjusted for the variables of sex, approximated age at the time of infection, region of origin and city size.

Table 3 Multivariable analysis of long-standing HIV infections including interaction term between GISD ¹ and city size (only MSM ²)							
n=6,511							
Countryside (<100k residents)				Town/Major city (>= 100k residents)			
n (%)†		aPR [95% CI]‡	p-value	n (%)†		aPR [95% CI]‡	p-value
234	(59.9%)	1		815	(62.2%)	1	
1,090	(64.7%)	1.09 [1.01, 1.18]	0.033	1,521	(60.4%)	0.97 [0.92, 1.03]	0.350
251	(68.8%)	1.16 [1.05, 1.28]	0.004	147	(61.8%)	1.00 [0.92, 1.09]	0.953
¹ GISD German Index of Socioeconomic Deprivation, ² MSM Men who have sex with men							
†Strata specific number and proportion of long-standing infections at the time of diagnosis.							
‡Prevalence ratios with corresponding 95% confidence intervals of long-standing infections at the time of diagnosis were calculated for the exposure variable GISD using multivariable Poisson regression with ZIP code cluster-robust error variance (standard errors were adjusted for 626 clusters). The model was stratified for MSM and adjusted for the variables of approximated age at the time of infection, region of origin and city size. For simplicity purposes, only strata specific effect estimates of the GISD conditional on countryside vs. town/major city are depicted. The effect estimates of the remaining covariates are nearly identical as presented in Table 2 in the MSM stratum.							

developed AIDS at the time of their diagnosis (aPR: 1.41, 95% CI 1.08-1.85) compared to MSM in less deprived countryside areas (Table 5), again no differences were observed among MSM from towns or major cities with different deprivation levels (Table 5).

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Table 4 Multivariable analysis of infections at the stage of AIDS stratified for transmission mode						
	n=3,113			n=8,198		
		MSM ²			HET ³	
	n (%)†	aPR [95% CI]‡	p-value	n (%)†	aPR [95% CI]‡	p-value
GISD ¹						
Low deprivation	253 (11.4%)	1		149 (16.5%)	1	
Medium deprivation	594 (11.5%)	0.98 [0.85, 1.13]	0.750	299 (16.2%)	0.99 [0.82, 1.19]	0.923
High deprivation	126 (15.6%)	1.21 [0.98, 1.50]	0.076	61 (16.8%)	1.05 [0.79, 1.40]	0.735
Sex						
Male	973 (11.9%)	1		195 (19.2%)	1	
Female		(omitted)		314 (15.0%)	0.72 [0.60, 0.86]	<0.001
Approx. age (time of infection)						
15 to 19	4 (3.5%)	0.26 [0.10, 0.89]	0.007	4 (5.8%)	0.40 [0.16, 1.02]	0.056
20 to 29	350 (12.1%)	0.94 [0.82, 1.07]	0.369	201 (19.0%)	1.31 [1.07, 1.60]	0.008
30 to 39	320 (12.8%)	1		155 (15.0%)	1	
40 to 49	218 (11.6%)	0.89 [0.76, 1.05]	0.185	90 (16.3%)	1.00 [0.78, 1.27]	0.975
50 to 59	66 (10.5%)	0.80 [0.62, 1.03]	0.082	46 (15.9%)	0.95 [0.68, 1.33]	0.761
60 to 69	15 (9.8%)	0.74 [0.45, 1.22]	0.243	12 (13.4%)	0.78 [0.45, 1.35]	0.371

>69	0 (0.0%)	(omitted)		1 (4.6%)	0.25 [0.04, 1.75]	0.165
Region of origin						
Western and Central Europe	896 (12.0%)	1		215 (17.5%)	1	
Asia and the Pacific	30 (14.9%)	1.26 [0.90, 1.76]	0.173	35 (26.3%)	1.57 [1.16, 2.12]	0.003
Caribbean	1 (3.7%)	0.31 [0.05, 2.15]	0.238	3 (15.8%)	0.90 [0.33, 2.49]	0.846
Eastern Europe and Central Asia	13 (12.6%)	1.05 [0.64, 1.71]	0.849	26 (15.3%)	0.90 [0.62, 1.31]	0.596
Latin America	15 (7.0%)	0.62 [0.38, 1.02]	0.059	5 (19.2%)	1.03 [0.47, 2.29]	0.935
Middle East and North Africa	5 (5.3%)	0.44 [0.19, 1.02]	0.057	11 (14.1%)	0.71 [0.38, 1.32]	0.278
North America	4 (9.8%)	0.88 [0.36, 2.17]	0.789	1 (25.0%)	1.45 [0.23, 9.01]	0.692
Sub-Saharan Africa	9 (12.9%)	1.08 [0.58, 2.01]	0.798	213 (14.7%)	0.79 [0.66, 0.95]	0.014
City size						
Countryside <100k res.	426 (14.1%)	1.37 [1.16, 1.64]	<0.001	253 (16.1%)	0.90 [0.73, 1.11]	0.333
Town 100k - <1 million res.	287 (11.4%)	1.13 [0.94, 1.35]	0.192	150 (16.2%)	0.94 [0.75, 1.17]	0.568
Major city >= 1 million res.	260 (9.9%)	1		106 (17.4%)	1	

¹ *GISD* German Index of Socioeconomic Deprivation, ² *MSM* Men who have sex with men,

³ *HET* Persons with heterosexual contact

†Strata specific number and proportion of infections at the stage of AIDS at the time of diagnosis.

‡Prevalence ratios with corresponding 95% confidence intervals of infections at the stage of AIDS at the time of diagnosis were calculated for the exposure variable *GISD* using stratified multivariable Poisson regression with ZIP code cluster-robust error variance (standard errors were adjusted for 644

clusters in the MSM stratum and 592 clusters in the HET stratum). The models were adjusted for the variables of sex, approximated age at the time of infection, region of origin and city size.

Table 5 Multivariable analysis of infections at the stage of AIDS including interaction term between GISD¹ and city size (only MSM²)

n=8,198						
Countryside (<100k residents)				Town/Major city (>= 100k residents)		
	n (%)†	aPR [95% CI]‡	p-value	n (%)†	aPR [95% CI]‡	p-value
GISD ¹						
Low deprivation	66 (12.3%)	1		187 (11.1%)	1	
Medium deprivation	268 (13.7%)	1.12 [0.88, 1.42]	0.373	326 (10.2%)	0.92 [0.77, 1.10]	0.348
High deprivation	92 (17.2%)	1.41 [1.08, 1.85]	0.013	34 (12.5%)	1.12 [0.75, 1.68]	0.587
¹ GISD German Index of Socioeconomic Deprivation, ² MSM Men who have sex with men						
†Strata specific number and proportion of infections at the stage of AIDS at the time of diagnosis.						
‡Prevalence ratios with corresponding 95% confidence intervals of infections at the stage of AIDS at the time of diagnosis were calculated for the exposure variable GISD using multivariable Poisson regression with ZIP code cluster-robust error variance (standard errors were adjusted for 644 clusters). The model was stratified for MSM and adjusted for the variables of approximated age at the time of infection, region of origin and city size. For simplicity purposes, only strata specific effect estimates of the GISD conditional on countryside vs. town/major city are depicted. The effect estimates of the remaining covariates are nearly identical as presented in Table 4 in the MSM stratum.						

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Discussion

This study investigated the impact of regional socioeconomic deprivation on late HIV diagnoses in Germany. The proportion of long-standing infections as well as AIDS at the time of diagnosis was somewhat higher in regions of high socioeconomic deprivation compared to regions with low and medium deprivation. The results of the stratified multivariable analyses showed that MSM living in highly deprived regions in the countryside were more likely to have a long-standing infection and also more likely to have already developed an AIDS-defining condition at the time of their diagnosis compared to MSM in less deprived countryside regions. This effect of deprivation was not observed among MSM who live in towns or major cities. Among persons who acquired HIV via heterosexual contact, no effect of regional socioeconomic deprivation on the timing of their diagnosis was observed. Since the proportion of late diagnoses was substantially higher in the heterosexual transmission group compared to MSM, the results suggest that persons with heterosexual contact are generally at a higher risk of presenting late irrespective of their socioeconomic background. The proportion of late diagnoses among MSM was lower, for this transmission group socioeconomic deprivation in regions in the countryside however appears to have an impact on the timing of HIV diagnosis.

Previous studies in the German context have mainly focused on the distribution of late HIV presentation by available sociodemographic data of the national case surveillance [28]. The findings of our study are consistent with these as the highest proportions of late diagnoses were also observed among persons with heterosexual contact, older age at the time of diagnosis and migrants from high-prevalence countries [12, 13, 28]. These patterns have remained stable over time and were also observed in other Western European and North American countries [11, 29-31]. The relationship between limited socioeconomic resources and HIV has found attention especially in research conducted in the US where several studies found that the prevalence of advanced HIV infections was higher in impoverished areas and that structural inequalities drove late diagnoses [17, 32-34].

The findings of our study therefore build on existing evidence with regard to the population groups who are more likely to be diagnosed at later stages of their HIV infection. It is assumed that persons with heterosexual contact often do not test for HIV due to a lower self-perception of risk as well as limited knowledge and stigma-related misconceptions about HIV [35]. At the same time, this low awareness of HIV in the heterosexual transmission group is also existent among health care providers, who as a result often do not consider an HIV infection even if indicator illnesses are present [36]. As MSM have been and still are the population group most affected by HIV in the Western context, health campaigns promoting early testing behaviours have predominantly targeted this group [13]. With respect to socioeconomic deprivation, this study's results also confirm the findings of previous research in other Western contexts, showing that late diagnoses are more prevalent in areas of high socioeconomic deprivation. This has been attributed to the fact that people with fewer socioeconomic resources generally have lower health literacy, are less likely to practice healthy behaviours and have worse access to treatment [33, 37, 38].

Our study's findings however provide new insights into the differences between the main transmission groups as well as the role of city size, seeing that after controlling for the confounding variables, an effect of socioeconomic deprivation was found in MSM from countryside areas but not in MSM from towns or bigger cities, and on the whole not in persons with heterosexual contact. A possible hypothesis might be that socioeconomic factors that are usually associated with health outcomes do not play a role among persons with heterosexual contact because the risk perception of HIV in this group is generally low and outweighs the expected impact of socioeconomic inequalities. HIV education traditionally had a stronger focus on MSM, which might explain why MSM on the other hand are affected by a lack of socioeconomic resources when it comes to HIV health outcomes. As the assessment of MSM who live in countryside versus urban areas showed that the observed effect among MSM was driven by persons from the countryside, it can be assumed that urban areas offer better support structures for this group. The fact that HIV checkpoints, specialised medical practices and MSM communities are more often located in towns and bigger cities [27, 39, 40] might help to offset the effect of socioeconomic deprivation for MSM in urban areas when it comes to the detection of HIV. These findings should be taken into consideration when developing strategies aimed at reducing the number of late HIV diagnoses in Germany. The results suggest that it is necessary to target persons with heterosexual contact irrespective of their socioeconomic background. Structural inequalities can be considered when MSM are addressed, with an increased focus on rural regions of higher socioeconomic deprivation for this population group.

A strength of this study is the utilisation of the GSD in the analysis of the impact of regional socioeconomic deprivation. As the score was calculated for each region nationwide, it was possible to match a score to every patient included in the analysis on the basis of the ZIP code, allowing to analyse the majority of all newly diagnosed HIV cases reported between 2011 and 2018. This comprehensiveness might not have been ensured if socioeconomic status had been indicated by the patients or respective doctors. In addition to that, the GSD has shown to be a reliable tool for the analysis of regional socioeconomic inequalities and health as statistical links were also found in prior research concerning life expectancy, major causes of death and various behavioural health risks in Germany [18, 41].

This study is also subject to limitations. Both outcome variables had missing values (see Table S1 and Table S2, Additional file 2) due to the fact that the BED-CEIA is not performed for all newly diagnosed cases and the CDC category not indicated in some cases. However, as the variables were reported by laboratories and physicians, it is presumed that there was no relationship between the probability of an outcome value being missing and the outcome itself, and hence no missingness pattern discernible that might have considerably affected the analysis. Another limitation is the fact that the GSD illustrates regional and not individual socioeconomic deprivation. It is therefore beyond the scope of this study to make claims about the impact of a person's individual socioeconomic status on late HIV presentation. Nevertheless, as risk factors regarding health outcomes are generally more prevalent in areas characterised by high levels of socioeconomic deprivation, regional socioeconomic factors have proven to serve as valid proxy variables for aggregated individual socioeconomic deprivation [18].

This study offers new findings and insights into the relationship of regional socioeconomic deprivation and late HIV presentation in the context of Germany. Further research that builds on these findings is therefore needed. We recommend that future studies also take individual socioeconomic factors into account. In order to gain a deeper understanding of the underlying dynamics, it would also be of interest to investigate which HIV health behaviours as well as structural factors related to the healthcare system are most affected by socioeconomic deprivation and how these could be best addressed.

Conclusions

This study has found that HIV infections which are diagnosed at long-standing and AIDS stages are somewhat more prevalent in areas characterised by high levels of socioeconomic deprivation. After having controlled for confounding variables, an effect of socioeconomic deprivation on the timing of HIV diagnosis was however found only among MSM from countryside areas. In order to tackle the burden of late HIV diagnoses in Germany, the findings suggest that efforts in promoting HIV awareness and regular testing behaviours have to be increased for heterosexual persons irrespective of their socioeconomic background. For MSM, we recommend that a focus is put on those living in rural regions of higher socioeconomic deprivation.

Declarations

Ethics approval and consent to participate

The “InzSurv-HIV” study has been approved by the data protection officer of the Robert Koch Institute and the Federal Commissioner for Data Protection and Freedom of Information (II-401/008#0016). Ethical approval for the monitoring of recent HIV infections was given by the ethics commission at the Charité – University Medicine Berlin (EA1/007/08). No patient informed consent was obtained as the data on new HIV diagnoses were derived from the national statutory HIV surveillance which is carried out in compliance with the German Infection Protection Act (IfSG). The samples used in the BED-CEIA assay were residuals from routine diagnostic processing. Recency testing of these samples is only licensed for epidemiological analyses and does not allow for individual patient analyses. All methods used in our study were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The HIV data analysed during the current study are not publicly available. They were generated from the national statutory notification of newly diagnosed HIV cases and blood samples which are directly sent and processed at the Robert Koch Institute. The dataset is available from the corresponding author on reasonable request.

The German Index of Socioeconomic Deprivation is publicly available and can be accessed via the GESIS repository, <http://doi.org/10.7802/1460>.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

AP, UK, BGB and VB designed the study. NB and KH were in charge of the BED-CEIA laboratory tests and provided the data. JH and NM conceived the GSD and provided the data as well as guidance on its use in health research. AP and UK coordinated the study and performed the analyses. MadH provided input for the statistical analyses. AP drafted the manuscript and all authors contributed to reviewing and revising the draft.

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