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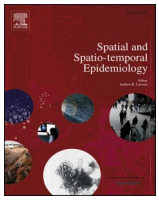

MSM with HIV: Improving prevalence and risk estimates by a Bayesian small area estimation modelling approach for public health service areas in the Netherlands

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ABSTRACT

Despite close monitoring of HIV infections amongst MSM (MSMHIV), the true prevalence can be masked for areas with small population density or lack of data. This study investigated the feasibility of small area estimation with a Bayesian approach to improve HIV surveillance. Data from EMIS-2017 (Dutch subsample, $n = 3{,}459$) and the Dutch survey SMS-2018 ($n = 5{,}653$) were utilized. We applied a frequentist calculation to compare the observed relative risk of MSMHIV per Public Health Services (GGD) region in the Netherlands and a Bayesian spatial analysis and ecological regression to quantify how spatial heterogeneity in HIV amongst MSM is related to determinants while accounting for spatial dependence to obtain more robust estimates. Both estimations converged and confirmed that the prevalence is heterogenous across the Netherlands with some GGD regions having a higher-than-average risk. Our Bayesian spatial analysis to assess the risk of MSMHIV was able to close data gaps and provide more robust prevalence and risk estimations.

1. Introduction

For epidemiology in men who have sex with men (MSM) with HIV (MSMHIV), data are often characterised by a spatial structure (Shrestha et al., 2020). However, most studies in the field often ignore these spatial characteristics. Examining the spatial structure with small area estimation (SAE) allows to identify high-risk spatial clusters of MSMHIV and to explore how these clusters relate to geographic characteristics (Meyers et al., 2014; Shrestha et al., 2020). Such an approach can be useful to assess areas of increased intervention need (Khan et al., 2020). Consequently, targeted interventions, from HIV testing, to HIV treatment linkage and adherence programmes, can be delivered more efficiently to accelerate ending HIV epidemic amongst this population as posited by UNAIDS (UNAIDS, 2021).

In the Netherlands, despite epidemiological reports of MSMHIV having been provided by Stichting HIV Monitoring (SHM, the Dutch HIV monitoring foundation) on the national level annually (van Sighem A.I., 2020), information on clusters of MSMHIV on a smaller geographical level, such as Public Health Services (GGD) regional level, are not available. Estimates on GGD level can provide valuable information for Dutch policymakers to better support local MSMHIV monitoring and prevention, as GGDs are independently responsible to provide healthcare services and prevention, and to monitor the general health of the local population. However, given the declining HIV epidemic amongst MSM in the Netherlands (van Sighem A.I., 2020), with a relatively small size of the MSM population in some GGDs in the Netherlands, crude calculation of MSMHIV prevalence and risk on GGS level can be misleading by chance. Hence, more advanced methodologies are required and should be applied to obtain robust estimates to monitor epidemic of MSMHIV on a finer geographical level, such as GGD level.

Bayesian spatial analysis is a well-established method for SAE, which allows assessment of spatial high-risk clusters, sharing of information across geographies, as well as prediction of estimates (Blangiardo et al., 2013; Goldstein et al., 2021; Wang et al., 2022). Compared to other different SAE techniques that had been applied in the field of HIV, such as generalized additive models (Wand et al., 2021), basic area-level models (Gutreuter et al., 2019), and Poisson regression models (Khan et al., 2020), Bayesian spatial analysis can additional account for a number of sources of error or bias, such as spatial autocorrelation between neighbouring spatial units and uncertainty due to instability of

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estimates in sparsely populated areas (Mouhanna et al., 2020). In addition, Bayesian spatial analysis also allows to evaluate socio-ecological facilitators and hurdles of MSMHIV jointly with spatial distribution to unravel co-variation (Blangiardo et al., 2013). As a result, how MSM-related determinants as regional characteristic, such as other sexualised transmitted infections (STIs) (den Daas et al., 2015; Wang et al., 2022), impact on the MSMHIV high-risk clusters in the Netherlands can also be explored. However, despite the advantages of Bayesian spatial analysis and applications in the context of HIV pre-exposure prophylaxis mapping (Mouhanna et al., 2020), it has not applied in monitoring MSMHIV in the Netherlands.

We thus aimed to apply Bayesian spatial analysis to identify high-risk clusters of MSMHIV on GGD regional level using two independent survey-based datasets on MSM in the Netherlands to investigate the applicability of spatial analysis modelling techniques to support future MSMHIV monitoring. In this study, we illustrated the posterior MSMHIV prevalence and high-risk clusters in the Netherlands. We also compared the spatial null and spatial ecological regression final models to assess the knowledge gap of how regional characteristics may impact on MSMHIV high-risk clusters in the Netherlands. As a secondary objective, we compared the results by two survey-based datasets to explore the stability and robustness of Bayesian spatial analysis.

2. Methodology

2.1. Study population and data sources

2.1.1. Study area

There are 25 Public Health Service institutions (GGD) in the Netherlands serving a specific region. The geographical structure of the Netherlands with boundary geoinformation of GGD regions was retrieved from Statistics Netherlands (CBS) (CBS, 2020) and linked with postal code datasets (CBS, 2017). Fig. 1 presented the spatial structure on region connectivity of the Netherlands on GGD regional level based on the common sharing of boarders.

2.1.2. EMIS-2017

All MSM included in this dataset were recruited between 19 October 2017 and 30 January 2018 via the European MSM Internet Survey (EMIS-2017, www.emis2017.eu) and were drawn from the Dutch subsample. EMIS-2017 was an anonymous, self-administered, and cross-sectional online survey conducted across 50 countries to inform interventions for MSM which are highly affected by infections with HIV and other STIs (Weatherburn et al., 2020). EMIS-2017 recruited 3851 MSM in the Netherlands. We excluded 392 (10.2%) men that failed to provide information on their place of residence (final dataset $n = 3459$). Ethical approval for this survey was obtained from the Observational Research Ethics Committee at the London School of Hygiene & Tropical

Fig 1. Region connectivity matrix of the Netherlands at the Public Health Services level
Note: for names and more details on the Public Health Services regions in the Netherlands, please see: https://www.ggd.nl/.

Medicine (14,421/RR/8805).

2.1.3. SMS-2018

The cross-sectional Survey Men & Sexuality (SMS-2018), led by Soa Aids Netherlands and Utrecht University, aimed to investigate the health, well-being, and sexuality of MSM in the Netherlands. It enroled MSM between February and June 2018 through social media, gay media and dating apps. The survey was distributed in six languages to include a culturally diverse sample of MSM. All participants had provided informed consent prior to accessing the survey (den Daas et al., 2018). SMS-2018 recruited 6206 MSM in the Netherlands. We excluded 552 (8.9%) men failed to provide their postal code (final dataset $n = 5654$). Ethical approval for this survey was obtained from the Ethics Committee of the Faculty of Social and Behavioural Sciences, Utrecht University (FETC17–131).

Data from two datasets were aggregated to the Public Health Services (GGD) regional level by the provided 2-digit postal code (4-digit postal code for SMS-2018) prior to the data analysis. Since the two surveys were conducted by two independent parties without a shared personal identifier, it was not possible to identify to which extent the two datasets overlapped with each other. We thus modelled these two datasets separately without combination, to avoid violating the independent observation assumption in our models, and to investigate the variability and applicability of HIV monitoring using survey-based data for our secondary objective of this study. However, we recommend investigating latent HIV prevalence with joint datasets whenever possible, given the Bayesian approach is known for its ability to produce updated posterior estimates with joint datasets (Peterson et al., 2021).

2.2. Small area estimation analysis

2.2.1. Frequentist analysis

We first calculated the observed MSMHIV prevalence per GGD region with its 95% confidence interval (95%CI) by dividing the MSMHIV count by the numbers of MSM inhabitants that participated in the surveys per region. We then calculated the standardized prevalence ratio (SPR) per GGD region, which is defined as the ratio of the observed counts to the expected counts using an indirect standardization approach, based on the overall risk of MSMHIV in the Netherlands (Becher and Winkler, 2017). As a spatial epidemiological measure, SPR could be applied to present the risk of MSMHIV per GGD region compared to the overall risk of HIV in the Netherlands on the regional/populational level. Put differently, that is to assess whether GGD region i has a higher (SPR >1), equal (SPR=1) or lower (SPR<1) risk than the overall risk in the total population (Wang et al., 2022; Webb et al., 2016).

2.2.2. Bayesian modelling (null model)

We further investigated the prevalence of MSMHIV by utilizing a Bayesian spatial model. We first conducted a null model accounting only for the spatial random effects and noises. To conduct the modelling analysis, we used the Integrated Nested Laplace Approximation (INLA), which is designed for latent Gaussian models, for the Bayesian computation (Rue et al., 2017). INLA allows models to be in the form:

$$y_i|\boldsymbol{x},\boldsymbol{\theta} \sim \pi(y_i|x_i,\boldsymbol{\theta}),\ i = 1,\ldots,n,$$

$$\boldsymbol{x}|\boldsymbol{\theta} \sim N\left(\boldsymbol{\mu}(\boldsymbol{\theta}),\boldsymbol{Q}(\boldsymbol{\theta})^{-1}\right),$$

$$\boldsymbol{\theta} \sim \pi(\boldsymbol{\theta}),$$

where y_i denotes the observation data, $\boldsymbol{x}$ represents a Gaussian field to model a spatially continuous variable underlying the observations, and $\boldsymbol{\theta}$ are hyperparameters, $\boldsymbol{\mu}(\boldsymbol{\theta})$ is the mean and $\boldsymbol{Q}(\boldsymbol{\theta})$ is the precision matrix of the latent Gaussian field $\boldsymbol{x}$ (Moraga, 2019).

For our counted outcome (HIV yes/no), following the suggestion by Diggle et al. (1983), we assumed that the observed HIV cases Y_i in each GGD region i in both aggregated datasets to follow a Poisson distribution (Diggle, 1983) with mean E_iRR_i, where E_i is the expected number which represents the total number of cases that one would expect if the population of GGD region i behaved the way the overall population behaves and was dependant on the number of participants who completed each survey in GGD region i and RR_i is the relative risk (RR) in each GGD region i:

$$Y_i \sim Po(E_iRR_i),\ i = 1,\ldots,N,$$

$$E_i = r^{(s)}n^{(i)},$$

where $r^{(s)}$ is the prevalence of MSMHIV in the overall participants (total number of MSMHIV divided by total participants in each survey on the Dutch national level), and $n^{(i)}$ is the number of participants of GGD region i.

We thus can define the RR on the logarithmic scale:

$$\log(RR_i) = \alpha + u_i + v_i$$

Where α represents the overall risk of MSMHIV in the Netherlands based on our assumption on E_i, u_i is a random effect on area i which is used to model spatial dependence between the RR, and v_i represents other unstructured noise which follows a distribution of $v_i \sim N(0,\sigma_v^2)$.

For the model parameters, we employed the re-parameterized Besag-York-Mollie (BYM2) model by Simpson et al. (2017), which specifies the spatially structured residual using an intrinsic conditional autoregressive (iCAR) distribution (Morris et al., 2019; Riebler et al., 2016). In addition, to specify the prior distribution for the Bayesian modelling, due to lack of information on GGD regions in the Netherlands, we assigned a weak, understandable, conservative and useful Penalized Complexity (PC) prior for the precision of the exchangeable random effects, which includes the random effects by using a scaled spatially structured component $\boldsymbol{u}_*$ and an unstructured component $\boldsymbol{v}_*$ (Simpson et al., 2017):

$$u_i + v_i = \boldsymbol{b} = \frac{1}{\sqrt{\tau_b}}\left(\sqrt{1-\phi}\,\boldsymbol{v}_* + \sqrt{\phi}\,\boldsymbol{u}_*\right)$$

Where $\boldsymbol{b}$ denotes the random effects, $\tau_b > 0$ is a marginal precision parameter contribution from spatial term $\boldsymbol{u}_*$ and random effect $\boldsymbol{v}_*$, and the fraction of this variance explained by the from spatial term $\boldsymbol{u}_*$ and random effect $\boldsymbol{v}_*$ are the mixing parameter $0 \le \phi \le 1$ (Simpson et al., 2017). To define the PC prior, we used the probability statement $P((1/\sqrt{\tau_b}) > U) = \alpha$. Based on the rule of thumb by Simpson et al. (2017), we set $U = 0.5/0.31$ and $\alpha = 0.01$. We then defined the prior for the mixing parameter ϕ as $P(\phi < 0.5) = 2/3$, which assumed that the unstructured random effect accounts for more of the variability than the spatially structured effects (Moraga, 2019).

2.2.3. Bayesian spatial ecological regression modelling (final model)

Additional to the null model, we hypothesised that MSMHIV across the Netherlands can be influenced by the established determinants of MSMHIV reported by den Daas et al. (2015) using EMIS-2010 datasets. These determinants included: prevalence of HIV testing (% ever tested); age (% >=35 years old); median number of sex partners; proportion of injecting drug users [(IDU),% IDU in EMIS-2017]/proportion of injecting drug use during sex [(SLAM),% SLAM in SMS-2018]; proportion of never using condom with last partner (% never); prevalence of syphilis (% yes), prevalence of chlamydia (% yes) and prevalence of gonorrhoea (% yes) in EMIS-2017 and prevalence of syphilis, chlamydia and gonorrhoea in the past 6 months in SMS-2018. Detailed definition of variables can be found in the published methodology paper for EMIS-2017 (Weatherburn et al., 2020), and SMS-2018 (den Daas et al., 2018). All spatial proxies listed above were also aggregated on the GGD regional level in both datasets.

We then applied a spatial ecological regression modelling technique (Blangiardo et al., 2013) which takes these selected determinants of MSMHIV into account separately by EMIS-2017 and SMS-2018. We first conducted univariable models which only include one of the selected regional determinants and the spatial connectivity:

$\log(RR_i) = \alpha + \beta_1 d_i + \boldsymbol{b}$, where d_i represent the one of the deteminants selected in this study and β_1 is the coefficients for the vector d_i. We conducted multivariable models with the significant determinants indicated by the univariable models to evaluate the impact on HIV prevalence in the Netherlands:

$$\log(RR_i) = \boldsymbol{d_i}\boldsymbol{\beta} + \boldsymbol{b},$$

$$\boldsymbol{d_i} = \left(1, d_{i1}, \ldots, d_{ip}\right)$$

$$\boldsymbol{\beta} = \left(\beta_0, \beta_1, \ldots, \beta_p\right)'.$$

We selected the final model using the backward approach by comparing models' Deviance Information Criterion (DIC), which is a somewhat Bayesian version of Akaike information criterion (AIC) (Gelman et al., 2014). The smaller DIC indicates a better goodness of fit of the model. Given our models are not highly dissimilar for model comparison, we regard using the DIC as sufficient, rather than using other more advanced fully Bayesian techniques, such as Watanabe-Akaike information criterion (WAIC) (Gelman et al., 2014), to estimate the goodness of fit of our models. Finally, we used the estimated median mixing parameter Phi (ϕ) for the spatial components, given the skewed distribution of the spatial effect, to evaluate the proportion of variance explained by the structured spatial component (Blangiardo et al., 2013). We quantified the spatial random effects per GGD region based on the spatial structure of the Netherlands to estimate the influence from the spatial structure of the Netherlands on the GGD regional level on HIV prevalence for both the null spatial model and the final spatial ecological regression model.

2.3. Computational analysis

All analyses were conducted in R (version 4.2.1). We used SpatialEpi R package (version 1.2.7) to estimate the expected MSMHIV number per GGD region per dataset Chen et al., 2021). For all Bayesian modelling analyses with INLA, we used R-INLA package (version 21.05.02) to empower our computational process (Blangiardo et al., 2013).

3. Results

3.1. Study population characteristics

Regional characteristics relevant to MSMHIV across the Netherlands were heterogenous for both datasets. For these established individual level determinants, HIV testing proportions ranged from 64.1% in GGD Drenthe to 92.3% in GGD Amsterdam in EMIS-2017 (and ranged from 62.7% in GGD Limburg-Noord to 92.7% in GGD Amsterdam in SMS-2018). Major differences between ever-/recent-diagnosed STIs proportion amongst Dutch MSM were observed from the two datasets. For ever diagnosed STIs proportion in EMIS-2017, ever diagnosed syphilis ranged from 10.3% in GGD Drenthe to 34.4% in GGD Zaanstreek/Waterland; and ever diagnosed chlamydia ranged from 19.7% in GGD Gelderland-Zuid to 45.2% in GGD Zaanstreek/Waterland. For recent diagnosed STIs (within six months) in SMS-2018, recently diagnosed syphilis ranged from 18.0% in GGD Drenthe to 44.4% in GGD Amsterdam. More detailed information for other regional characteristics (older than 35 years proportion, IDU proportion, and other STIs) per GGD region from both datasets can be found in Online resource S1 table.

3.2. Frequentist observed MSMHIV prevalence and risk

In terms of the prevalence of MSMHIV in the Netherlands, the observed overall prevalence of HIV amongst MSM in 2017 was 14.2% in EMIS-2017 and 9.5% in SMS-2018. In EMIS-2017, the observed prevalence of HIV varied by GGD regions in the Netherlands, with a range of 6.8% (95%CI 3.16–14.09) in GGD Limburg Noord to 25.0% (95%CI 13.25–42.11) in GGD Zaanstreek/Waterland. In SMS-2018, the observed prevalence varied from 3.7% (95%CI 1.59–8.38) in Veiligheids- en Gezondheidsregio Gelderland-Midden (VGGM) to 14.15% (95%CI 11.67–17.06) in GGD Amsterdam (Fig. 2a & 2d, Online resource S2 table). The crude SPR in Fig. 3-a and 3-d shows that regions with higher-than-average risk of HIV exist in the Netherlands, with a range of 0.43 (GGD Limburg Noord) to 1.59 (GGD Zaanstreek/Waterland) in EMIS-2017; and 0.39 (VGGM) to 1.49 (GGD Amsterdam) in SMS-2018. The SPR trends corresponded with the patterns of the observed HIV prevalence. More detailed information for the frequentist observed prevalence and SPR of MSMHIV can be found in Online resource S2 table.

3.3. MSMHIV prevalence and risk after Bayesian spatial adjustment

After accounting for the spatial effects based on the spatial structure of the Netherlands on the GGD region level presented in Fig. 1 without other regional determinants of HIV transmission, the EMIS-2017′s Phi of the spatial structure was estimated at 0.24, which indicates that around 24% of the observed variance of HIV amongst MSM in the Netherlands can be explained by the spatial structure of the Netherlands on the GGD regional level, and the SMS-2018′s Phi was 0.27 (Table 1).

As indicated by the observed HIV prevalence, we observed heterogeneity of the posterior HIV prevalence in the Netherlands estimated by the spatial null models in both datasets. In EMIS-2017, the highest posterior HIV prevalence was found in the GGD Amsterdam of 18.6% (95%CrI 15.87–21.58) and the lowest in GGD Limburg-Noord of 11.7% (95%CrI 7.2–16.4). GGD Amsterdam was estimated as the only region with statistically significant higher-than-average risk of HIV amongst MSM in the Netherlands with a RR of 1.18 (95%CrI 1.01–1.37). Full details of all GGD regions according to the spatial null model can be found in Online resource Table S2 and Fig. 3-b. In SMS-2018, the posterior prevalence and RR was the similar as the observed prevalence, the highest posterior HIV prevalence was found in Amsterdam, too, of 12.16% (95%CrI 9.58–15.14) with the only significant higher-than-average risk of HIV of 1.28 (95%CrI 1.01–1.59), and the lowest in VGGM of 8% (95%CrI 5.09–10.69) with RR of 0.84 (95%CrI 0.54–1.13), see Fig. 3-e and Online resource S2 table.

Posterior spatial random effects on the HIV prevalence estimated by the null model can be found in Fig. 4-a and 4-c, which confirms the spatial heterogeneity and indicates how the spatial structure impacts on the estimated posterior RR per GGD region, with a range of [EMIS-2017: −0.21 (GGD Limburg-Noord) to 0.27 (GGD Amsterdam)] and [SMS-2018: −0.15 (VGGM) to 0.28 (GGD Amsterdam)]. In other words, regions with a positive (or negative) value of the spatial random effects indicate having an elevated (or lower) relative risk of HIV than the overall risk in the Netherlands.

3.4. MSMHIV prevalence and risk after Bayesian spatial ecological adjustment

3.4.1. Univariable models

In EMIS-2017, after adjusting on the observed HIV testing prevalence as the regional determinant, a coefficient of 2.72 (95%CrI 0.61–4.73, DIC=144.42, Phi=0.27) was modelled. This means that each increase of one percent in HIV testing prevalence in a region is associated with an increase of around 2.8% (=exp(2.724×0.01)) in HIV risk in that region. The coefficient for the observed syphilis prevalence was estimated at 3.55 (95%CrI 1.26–5.70, DIC=142.41, Phi=0.28), which indicated that for every one percent increase of the regional prevalence of syphilis, the

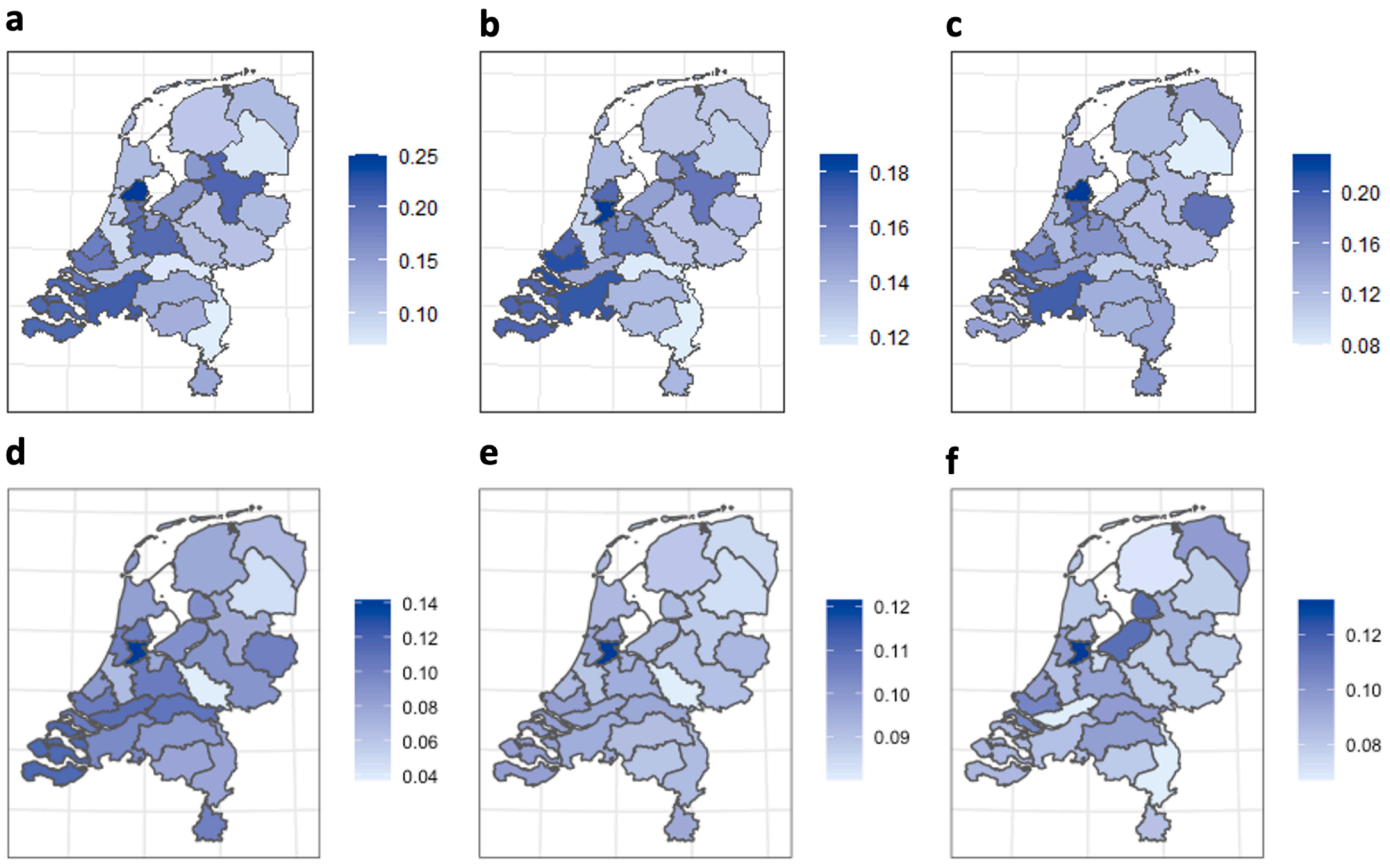

Fig 2. Choropleth map of the estimates of MSMHIV prevalence by GGD regions in the Netherlands.
"A: Observed HIV prevalence by EMIS-2017. B: Posterior mean of HIV prevalence estimated by Bayesian spatial modelling (null model) by EMIS-2017. C: Posterior mean of HIV prevalence estimated by Bayesian spatial ecological regression modelling (final model) by EMIS-2017. D: Observed HIV prevalence by SMS-2018. E: Posterior mean of HIV prevalence estimated by Bayesian spatial modelling (null model) by SMS-2018. F: Posterior mean of HIV prevalence estimated by Bayesian spatial ecological regression modelling (final model) by SMS-2018. See Online resource Table S2 for the 95%CI or 95%CrI and other details.
Notes: the darker a GGD region, the higher the prevalence estimation of HIV amongst MSM.

regional risk of HIV increases by 3.5%. Similar for gonorrhoea, the increased risk was 2.3%. The other areal determinants of HIV (age, number of partners, condom use, IDU prevalence and chlamydia prevalence) were not significantly associated with the posterior mean of RR of HIV in the Netherlands (Table 1).

In SMS-2018, we observed a significant positive association between HIV test and MSMHIV with a coefficient of 2.67 (95%CrI 0.74–4.50, Phi=0.31, DIC=118.97) in the univariable model. In addition, instead of STIs' spatial prevalence, we found that proportion of higher age, coefficient=2.45 (95%CrI 0.55–4.23, Phi=0.28, DIC=119.84) and proportion of never using a condom with non-steady partners, coefficient=3.12 (95%CrI 0.36–5.62, Phi=0.29, DIC=121.04) were positively associated with the MSMHIV risk on the GGD regional level. Other areal characteristics of GGD regions were not estimated significant within this dataset (Table 1).

3.4.2. *Multivariable models (final model)*

After conditioning significant areal characteristics of MSMHIV, and selecting by the smallest DIC, in EMIS-2017, the final model included HIV testing prevalence with a coefficient of 1.60 (95%CrI −0.60–3.74) and syphilis prevalence with a coefficient of 2.67 (95%CrI 0.19–5.10), a DIC of 141.74, and a Phi of 0.28. The coefficients' estimations indicate that both univariable models of HIV testing, and ever-diagnosed syphilis prevalence overestimated the effects from these two regional determinants of HIV. Even though HIV testing was not statistically significant in the final model, the DIC of the final model was smaller than the DIC of the model with only syphilis prevalence (DIC=142.41). Therefore, we kept HIV testing in the final model (Table 1). In the multivariable model based on SMS-2018, we included HIV testing prevalence with coefficient=1.80 (95%CrI −0.29–3.94) and proportion of higher age with coefficient=1.515 (95%CrI −0.55–3.57) with the smallest DIC of 118.58 and a Phi of 0.30 in the final model (Table 1).

The posterior prevalence of MSMHIV was again heterogenous in both datasets. In EMIS-2017, the highest posterior prevalence of MSMHIV was observed from GGD Zaanstreek/Waterland of 22.9% (95% CrI 16.25–30.8), and the lowest posterior prevalence of HIV was observed from GGD Drenthe of 7.89% (95%CrI 4.94–12.02). In addition, the final model succeeded to pick up the regions with higher-than-average risk of MSMHIV in the Netherlands other than GGD Amsterdam (RR=1.21, 95%CrI 1.05–1.38): GGD Rotterdam-Rijnmond (RR=1.19, 95%CrI 1.00–1.41) and GGD Zaanstreek/Waterland (RR=1.46, 95%CrI 1.04–1.96). Also, the risk of MSMHIV of GGD Noorden Oost-Gelderland (RR=0.72, 95%CrI 0.54–0.94), GGD Fryslân (RR=0.76, 95%CrI 0.57–0.98), GGD Drenthe (RR=0.5, 95%CrI 0.31–0.77) and GGD Hollands-Midden (RR=0.79, 95%CrI 0.58–0.99) were found to be significantly lower than the risk on the average level in the Netherlands. In SMS-2018, the lowest posterior MSMHIV prevalence was estimated in Dienst Gezondheid & Jeugd ZHZ of 6.71% (95%CrI 4.69–9.47) with a RR of 0.71 (95%CrI 0.49–1.00) and GGD Limburg-Noord of 6.71% (95%CrI 3.46–11.42) with a RR of 0.71 (95%CrI 0.36–1.20). The highest posterior prevalence was again observed in GGD Amsterdam: 13.25% (95%CrI 10.84–15.93), and it was the only one GGD region with a significant higher-than-average risk of MSMHIV in the Netherlands (RR=1.39, 95%CrI 1.14–1.68). For full details of

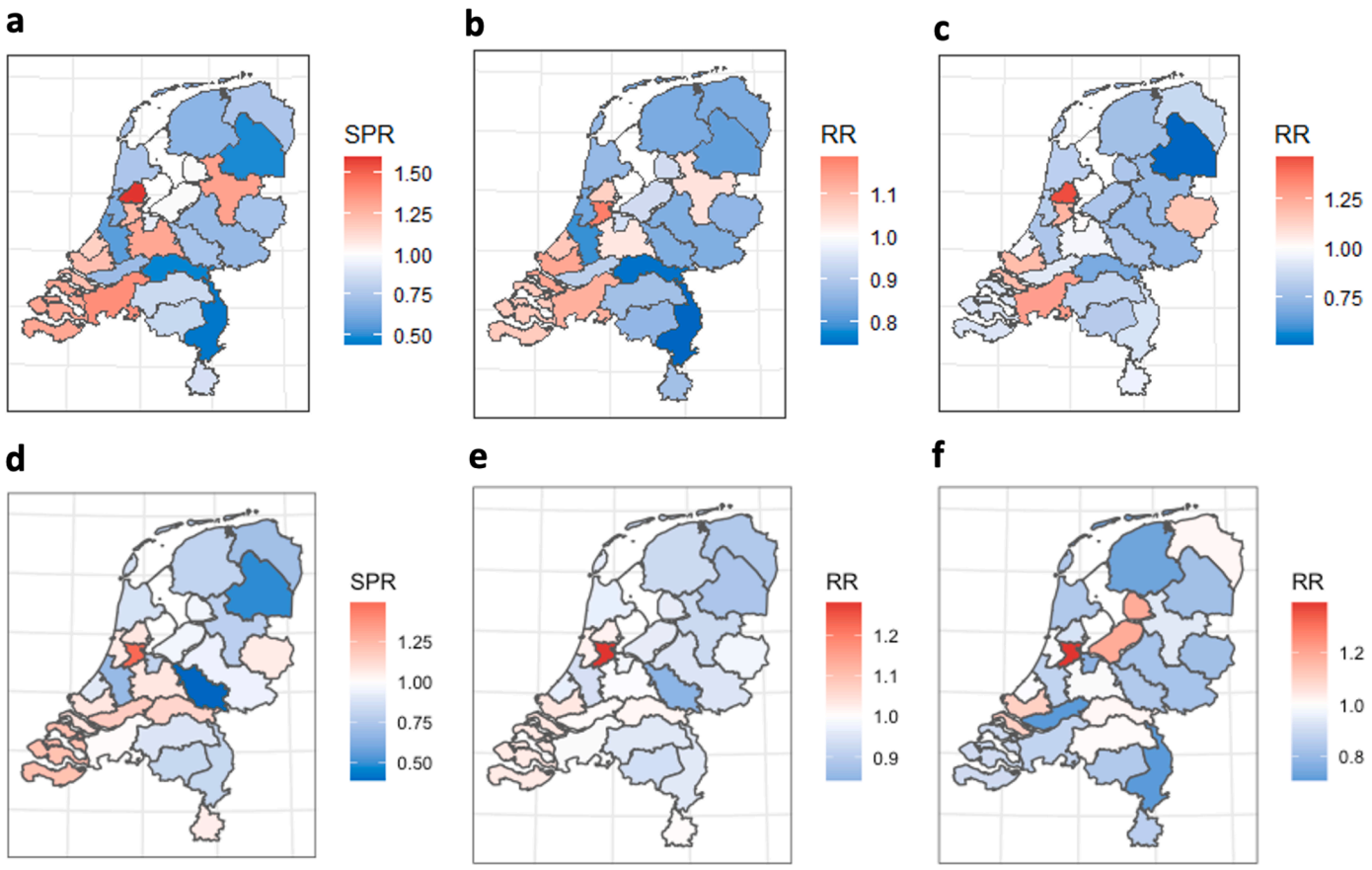

Fig 3. Choropleth map of the estimates of MSMHIV risks by GGD regions in the Netherlands.
A: Observed HIV standardised prevalence ratio by EMIS-2017. B: Posterior mean of HIV relative risk estimated by the Bayesian spatial modelling (null model) by EMIS-2017. C: Posterior mean of HIV relative risk estimated by the Bayesian spatial ecological regression modelling (final model) by EMIS-2017. D: Observed HIV standardised prevalence ratio by SMS-2018. E: Posterior mean of HIV relative risk estimated by the Bayesian spatial modelling (null model) by SMS-2018. F: Posterior mean of HIV relative risk estimated by the Bayesian spatial ecological regression modelling (final model) by SMS-2018. See Online resource Table S2 for the 95%CI or 95%CrI and other details.
Notes: RR (or SPR) higher than 1 indicates a higher-than-average (average risk in the Netherlands) risk of HIV amongst MSM in that region (red); RR (or SPR) lower than 1 indicates a lower-than-average risk of HIV amongst MSM in that region (blue).

posterior MSMHIV prevalence and RR per GGD region, see Online resource Table S2 and Fig. 3-c and 3-f.

The spatial random effects indicated again the heterogeneity on the RR of MSMHIV across the Netherlands with a range of [EMIS-2017: −0.08 (GGD Limburg Noord) to 0.08 (GGD Ijsselland); SMS-2018: −0.04 (VGGM) to 0.04 (GGD Amsterdam)]. The posterior spatial random effect per GGD region were summarised in Online resource Table S2 and Fig. 4-b and 4-d.

3.5. *Differences between estimations by EMIS-2017 and SMS-2018*

Despite the large overlap of the spatial pattern of MSMHIV by our analysis based on EMIS-2017 and SMS-2018 datasets, we found some minor differences in terms of both the observed and estimated posterior prevalence, which is generally lower in SMS-2018 data compared to EMIS-2017 data. One reason that may explain this finding is that the collection methods and processes were different between the SMS-2018 and EMIS-2017. However, in terms of the posterior relative risk of HIV on the GGD regional level, the results between these two datasets converged and reflect how the regional risks vary between different GGD regions on the national scale. The converged posterior RR estimations by both datasets indicated the strong stability of the Bayesian spatial analysis to identify regions with higher risk and subsequently for differentiated prevention allocation strategies.

We also observed a different impact of the areal determinants on our HIV prevalence and risk modelling between these two datasets. Despite the discussed sampling variations, different definitions of the determinants when collecting data through the surveys could also explain why our univariable models and final models are not fully overlapping. For example, in EMIS-2017, men were asked if they were ever diagnosed with any type of STI versus STI diagnosis within the past six months, as in SMS-2018. The HIV-risk profile and sexual behaviour profile of MSM would thus be different and result in a different impact on the ecological modelling analysis. Therefore, based on our findings in the univariable models, we could also conclude that the impact of the lifetime STI diagnoses should be greater than the recent STI diagnoses.

4. Discussion

To illustrate the applicability of Bayesian spatial analysis in MSMHIV monitoring in the Netherlands, we investigated the spatial high-risk clusters of MSMHIV in conjunction with regional characteristics relevant to MSMHIV using two survey data from the Netherlands at the level of the Public Health Services (GGD) regions.

Based on both datasets, we observed a heterogenous spatial high-risk clusters of MSMHIV. In particular, the GGD Amsterdam region and GGD Zeeland, had a significantly higher-than-average risk of MSMHIV in the Netherlands. The effect for the GGD Amsterdam region did not come unexpected, the effect for GGD Zeeland did. Jointly with the spatial patterns, we identified regional characteristics to be significantly

Table 1
Model comparison and selection for EMIS-2017 and SMS-2018.

Models	HIV diagnosis EMIS-2017 Covariates	Coefficient	95%CrI	DIC	Phi (ϕ) (95% CrI)	SMS-2018 Covariates	Coefficient	95%CrI	DIC	Phi (ϕ) (95% CrI)
Spatial Null model	Intercept	−0.108	(−0.257 – 0.025)	145.71	0.24 (0.01 – 0.77)	Intercept	−0.041	(−0.196 – 0.098)	123.99	0.27 (0.01 – 0.84)
Spatial Univariable models	Intercept	−2.359	(−4.052 - −0.597)	144.42	0.27 (0.01 – 0.87)	Intercept	−2.206	(−3.729 - −2.217)	118.97	0.31 (0.01 – 0.90)
	HIV test (%yes)*	2.724	(0.611 – 4.725)			HIV test (%yes)*	2.674	(0.738 – 4.501)		
	Intercept	−0.591	(−1.376 – 0.172)	145.89	0.24 (0.01 – 0.76)	Intercept	−1.166	(−2.027 - −0.271)	119.84	0.28 (0.01 – 0.84)
	Age (%>= 35 y. o.)	1.089	(−0.613 – 2.786)			Age (%>= 35 y. o.)*	2.454	(0.551 – 4.229)		
	Intercept	−0.063	(−0.232 – 0.083)	147.26	0.26 (0.01 – 0.83)	Intercept	0.073	(−0.498 – 0.645)	125.66	0.27 (0.01 – 0.81)
	Partner	−0.037	(−0.104 – 0.032)			Partner	−0.049	(−0.297 – 0.186)		
	Intercept	−5.305	(−10.373 – 0.715)	144.51	0.25 (0.01 – 0.81)	Intercept	−0.971	(−1.763 - −0.130)	121.04	0.29 (0.01 – 0.86)
	Condom (% never)	41.315	(−6.485 – 81.421)			Condom (% never)*	3.121	(0.359 – 5.622)		
	Intercept	−0.398	(−0.752 - −0.056)	145.51	0.32 (0.01 – 0.90)	Intercept	0.005	(−0.235 – 0.227)	125.47	0.27 (0.01 – 0.85)
	IDU (%yes)	4.41	(−0.369 – 9.051)			SLAM (%yes)	−0.561	(−2.812 – 1.601)		
	Intercept	−0.87	(−1.384 - −0.352)	142.41	0.28 (0.01 – 0.88)	Intercept	−0.049	(−0.327 – 0.220)	125.62	0.27 (0.01 −0.82)
	Syphilis (%yes)*	3.546	(1.263 – 5.703)			Syphilis (%yes) #	0.251	(−8.189 – 8.139)		
	Intercept	−0.662	(−1.281 - −0.029)	146.6	0.24 (0.01 – 0.81)	Intercept	−0.197	(−0.651 – 0.248)	125.42	0.29 (0.01 – 0.89)
	Chlamydia (% yes)	1.724	(−0.200 – 3.514)			Chlamydia (% yes)#	1.992	(−3.513 – 7.301)		
	Intercept	−0.856	(−1.552 - −0.132)	145.8	0.26 (0.01 – 0.83)	Intercept	−0.125	(−0.533 – 0.277)	125.64	0.27 (0.01 – 0.85)
	Gonorrhoea (% yes)*	2.255	(0.116 – 4.221)			Gonorrhoea (% yes)#	1.195	(−4.376 – 6.498)		
Spatial Multivariable final model	Intercept	−2.021	(−3.624 - −0.358)	141.74	0.28 (0.01 – 0.85)	Intercept	−2.225	(−3.701 - −0.739)	118.58	0.30 (0.01 – 0.90)
	HIV test (%yes)	1.607	(−0.6 – 3.737)			HIV test (%yes)	1.801	(−0.286 – 3.941)		
	Syphilis (%yes)	2.674	(0.192 – 5.099)			Age (%>= 35 y. o.)	1.515	(−0.549 – 3.571)		

Note: * = significant areal determinants of the univariable models. Partner = median number of partners. Condom =% never used condom with non-steady partners. # Indicates six-month prevalence instead of life-time prevalence. CrI = credible interval. DIC=Deviance Information Criterion.

associated with MSMHIV risk in the Netherlands. Methodologically, we found that the observed prevalence estimated by the frequentist analysis was less stable than the posterior prevalence estimated by the Bayesian spatial modelling in terms of the estimations range and their uncertainty range (the 95% confidence interval and 95% credible interval), especially for regions with smaller sample sizes. Despite a largely overlapping spatial high-risk clusters of MSMHIV in the Netherlands (both Frequentist observed, and Bayesian smoothed) between the two datasets, differences in the prevalence and spatial random effects were obtained.

4.1. Spatial at-risk clusters of MSMHIV in the Netherlands

Overall, based on the overlapping results from both datasets, we observed a higher prevalence of HIV in the West of the Netherlands where also the main urban areas (in Dutch: Randstad) are located, and in the GGD region of Zeeland, which belongs to the area that has the highest concentration of conservative orthodox Calvinist Protestants in the country (CBS, 2014).

It was within our expectation that the prevalence and risk of MSMHIV was higher in the GGD regions in the Randstad, such as GGD Amsterdam. This prevalence is also in line with findings from previous studies using surveillance data by geographic information system and survey-based data (den Daas et al., 2015; Op de Coul et al., 2017). In

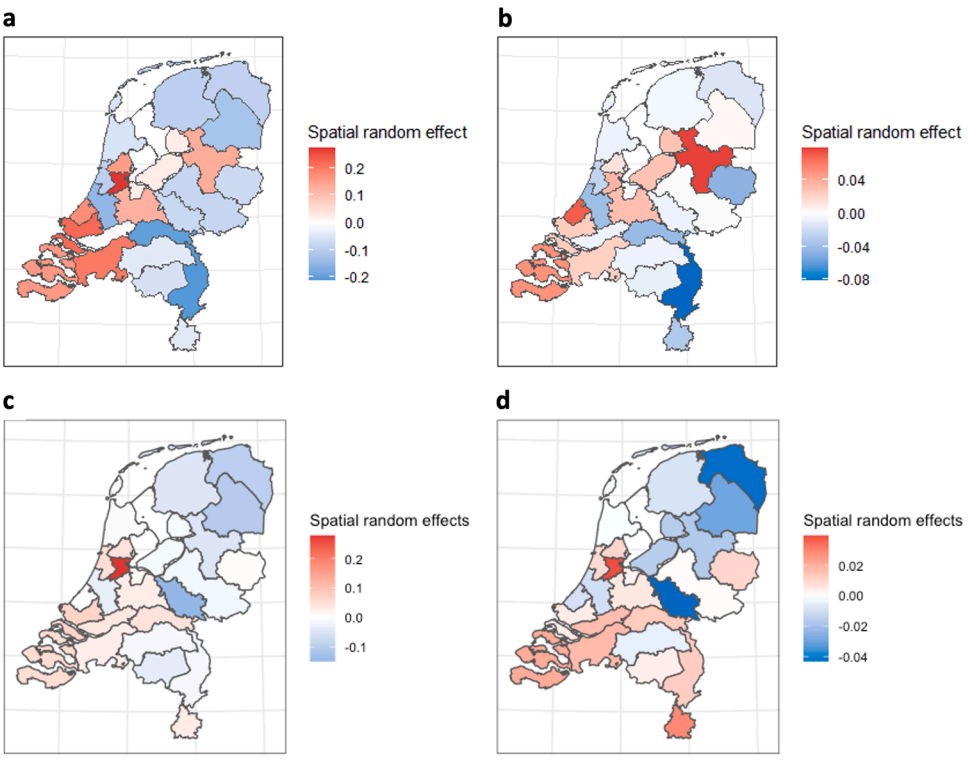

Fig 4. Posterior spatial random effects on the GGD regional level in the Netherlands.
A: posterior spatial random effects estimated by Bayesian spatial modelling (null model) by EMIS-2017. B: Posterior spatial random effects estimated by the Bayesian spatial ecological regression modelling (final model) by EMIS-2017. C: posterior spatial random effects estimated by Bayesian spatial modelling (null model) by SMS-2018. D: Posterior spatial random effects estimated by the Bayesian spatial ecological regression modelling (final model) by SMS-2018. See Online resource Table S2 for the 95%CrI and other details.
Notes: for spatial null model, regions with a positive (negative) value of the spatial random effects indicate having an elevated (lower) relative risk of HIV amongst MSM than the overall risk in the Netherlands.

addition, our analysis based on both datasets suggested a significant higher-than-average risk of MSMHIV in this GGD region compared to other regions in the Netherlands. Few reasons may explain our findings. Firstly, Amsterdam which is known as the 'Gay Capital of Europe' is the target of "gay tourism", with more sexual encounters occurring subsequently (Richards and Wilson, 2007). Likewise, more Dutch MSM choose to relocate to these main urban areas (den Daas et al., 2018), and the HIV cases would, therefore, be concentrated there as well. Another reason that contributed to a higher HIV prevalence is the high HIV testing rate amongst MSM in GGD Amsterdam region (Online resource S1 table). Our ecological modelling analysis also confirmed this argument that with a higher HIV testing prevalence, the risk of MSMHIV would be higher as well (Table 1).

It was, however, not expected that the GGD Zeeland also had a higher spatial risk (random effect, Fig. 4) of MSMHIV compared to other regions. One reason for this higher risk found for this region may be due to the religion/local culture. As one of the most conservative regions in the country with associated negative views on same-sex sexual activities and relations, an overall negative attitude towards homosexuality may be greater than in other regions (Keuzenkamp, 2011). In turn, some sexual behaviours may be stigmatized and MSM may experience more barriers to HIV testing, which may influence the risk of MSMHIV at that region: according to both datasets GGD Zeeland has one of the lowest HIV test prevalence amongst MSM (Online resource S1 table). Second, a longer distance to the STI clinics could play a role as a barrier to HIV testing in GGD Zeeland (Twisk et al., 2021), which could also leave an influence on the spatial high-risk clusters of MSMHIV in the Netherlands. Therefore, future studies should also investigate the distance to the STI clinics as a regional characteristic for a more comprehensive model.

4.2. *Applicability of Bayesian spatial modelling analysis*

The application of Bayesian spatial analysis in two survey-based datasets from the Netherlands provided evidence that monitoring the MSMHIV high-risk clusters with a Bayesian spatial analysis is applicable. Compared to calculating the observed crude prevalence and SPR, results of the posterior prevalence and risks estimations were smoother and more stable due to the narrower credible intervals estimated by INLA, which has been proven helpful to estimate the more accurate prevalence and risk as an approximation approach (Blangiardo et al., 2013). This approach increases certainty when interpreting the results and tailoring prevention programming for MSMHIV.

In addition, our spatial ecological modelling allowed us to investigate the variations of MSMHIV together with other regional characteristics of MSMHIV while the spatial components included in the spatial null model could not pick up these additional associations and noise. We found several regional characteristics (Table 1) based on our survey data useful to estimate the posterior prevalence and risk of MSMHIV in the Netherlands. Consequently, both two final models for EMIS-2017 and SMS-2018 data improved the goodness of fit after adding the regional determinants related to MSMHIV. Therefore, the established spatial characteristics relevant to MSMHIV high-risk clusters from this study should be considered valuable for policymakers and HIV monitoring authorities. Attention should be also given to these regional MSMHIV characteristics, too, instead of focussing on the numerical prevalence only.

We thus recommend promoting Bayesian spatial analysis as a statistical adjustment for future MSMHIV national/local surveillance and service navigation. Not only in the Netherlands, but also for the countries/settings with similar declining MSMHIV epidemic, this method can be useful and applicable, especially when there are gaps due to missing data, or regional prevalence estimates are needed, to identify high-risk clusters of MSMHIV to reach out the marginalised population with a more targeted intervention strategy. Even though we acknowledge that the complex statistical computation, unfamiliarity and limited knowledge on Bayes' Theorem may limit the application of this methodology for non-Bayesian stakeholders, the already available techniques and the various forms of open source statistical software (Blangiardo et al., 2013; Li et al., 2020; Lunn et al., 2000) should help to ease the computation process and help interpreting results.

4.3. Strength and limitations

We acknowledge the following strengths and limitations of our study. One major strength of this study is the introduction and the application of Bayesian spatial analysis. We considered our results, especially the posterior risks of MSMHIV, as robust and valuable for MSMHIV related public health policies and prevention strategies. The methodology used in our study can be directly applied in other countries in the future for SAE using surveillance data on MSMHIV. Another strength is the convergence of the models based on data from two independent survey-based datasets. Data from these two surveys made MSM individual level covariates directly available for the posterior modelling analysis instead of using secondary area-level covariate data based on the Dutch general population. Moreover, presenting data on the GGD regional level also helped to prevent information bias due to the municipal location of HIV testing. Since the regional GGDs run the majority of HIV tests in the Netherlands and since the sexual health clinics are located in the larger municipalities in a GGD region, data may thus concentrate in these bigger cities if HIV amongst MSM would be assessed on the municipality level.

In addition to the aforementioned limitations, one limitation can be the lack of data from the neighbouring regions from other countries. Our Bayesian spatial analysis with a hierarchical structure revealed how regions may influence each other to smoothen the risk estimates based on neighbouring information or on proximity. However, given the smoothing by neighbouring regions, our analysis may be influenced by other regions outside the Netherlands and may be influenced by the size of the population as well. It should be stressed that for some GGD regions which are located in the border regions of the Netherlands, the estimated prevalence and risks of HIV of these regions would thus be less stable and with more uncertainties compared to the rest due to the lower predictability as only one other node is available and thus part of spatial information is missing. Regions that share a boarder with Germany and Belgium, especially for GGD Zuid-Limburg which is only geographically connected with GGD Limburg-Noord and without other neighbouring regions in the Netherlands (Fig. 1), require additional cross-border data input. Therefore, a study including those neighbouring regions in Belgium and Germany may be warranted in the future to compensate for the problem of lack of national spatial connectivity for those boarder regions. To achieve this aim, comparable cross-border data needs to be accessible, too. Moreover, our spatial analysis of MSMHIV across the Netherlands was based on survey data from 2017 to 2018 when the pre-exposure prophylaxis (PrEP) has yet to be formally introduced in the Netherlands (2019). Our spatial model, therefore, did not include PrEP use amongst MSM per GGD region as a regional characteristic. Consequently, the influence from PrEP use was not measured in our models. Given the established impacted on the HIV prevention amongst MSM from using PrEP (Grant et al., 2014, 2010; Hoornenborg et al., 2019, 2017; McCormack et al., 2016), future studies should therefore include PrEP use into the spatial models for a more robust estimation. Another limitation can be the lack of an informative prior distribution when conducting Bayesian spatial analysis. Previous studies which applied Bayesian statistic in other epidemiologic field has suggested that to acquire the true prevalence and RR, an informative prior is preferred and required in practice (Goldstein et al., 2021; Lemoine, 2019). Our application of the PC prior, as a weakly informative prior, may thus limit the robustness of our posterior estimation and make them conservative (Lemoine, 2019). However, we believe our estimations were still robust and close to the true risk of HIV amongst MSM based on the previous sensitivity analysis of PC in a prior experiment (Simpson et al., 2017). In addition, even though our Bayesian approach made our estimations more robust, more comprehensive datasets, such as routine surveillance data are still warranted. Another major limitation in our study may be the lack of temporal dimension in our models. The scope of our study to offer a time-dynamic epidemiologic picture on how MSMHIV spatially distribute over the time is limited. Future studies thus should include a wide temporal period to support a more comprehensive spatio-temporal analysis. Finally, ecological fallacy is possible due to our ecological study design. We lose information on the individual-level due to aggregating information spatially. Our results on the roles of the regional characteristics thus cannot be directly applied to investigate/predict the MSM's HIV risk profile on the individual level.

5. Conclusions

In conclusion, our study proposed a Bayesian spatial analysis to more accurately assess the risk of MSMHIV using data from the Netherlands on the public health service regional level with more robust prevalence and risk estimations over the use of crude proportions. Our findings based on two independent surveys can be considered valuable for policymakers and HIV monitoring authorities for resources and service navigation decision by prioritizing resources to the regions which require more efforts to reduce the burden of MSMHIV accordingly. Based on the Dutch data, our method has shown to be applicable and feasible and can be directly applied to achieve a more comprehensive and robust surveillance of MSMHIV in any geographic context.

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Author contributions

All authors contributed to the study conception and design. Material preparation, data analysis were performed by [Kai J Jonas], [Chantal den Daas], and [Haoyi Wang]. The first draft of the manuscript was written by [Haoyi Wang] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Observational Research Ethics Committee at the London School of Hygiene & Tropical Medicine (review reference 14,421/RR/8805) and the Ethics Committee of the Faculty of Social and Behavioural Sciences, Utrecht University (FETC17–131).

Consent to participate

Informed consent was obtained from all individual participants included in the studies.

Declaration of Competing Interest

The authors have no relevant financial or non-financial interests to disclose.

Data availability

The authors do not have permission to share data.

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Supplementary materials

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