Spatial Epidemiology of Genital Ulcer Diseases Caused by HSV-1 and HSV-2, France, January 2022-December 2024

Olivier Supplisson*, Camille D'Humières, Benoit Visseaux, Stéphanie Haïm Boukobza, David Boutolleau, Samuel Alizon, Sonia Burrel, and Mircea T. Sofonea

Les cartes qui ont changé le monde (1/5) : John Snow, l'ancêtre des cartes du Covid-19

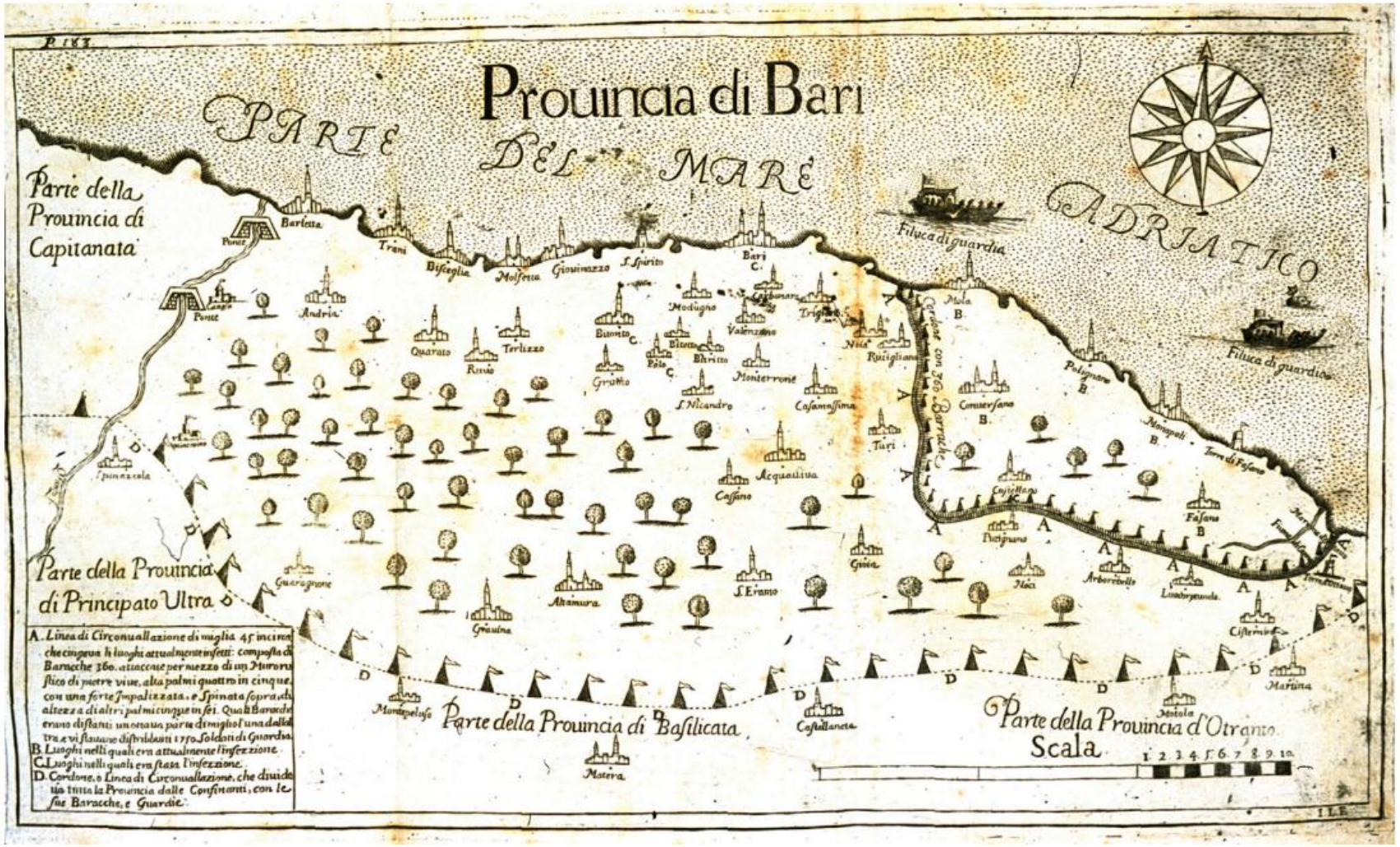
Série d'été. La carte du médecin John Snow (1813-1858) raconte celle de choléra de 1854 dans le quartier londonien de Soho, où il exerçait. Avec John Snow, la cartographie devient alors un allié de l'épidémiologie.

John Snow's data journalism: the cholera map that changed the world

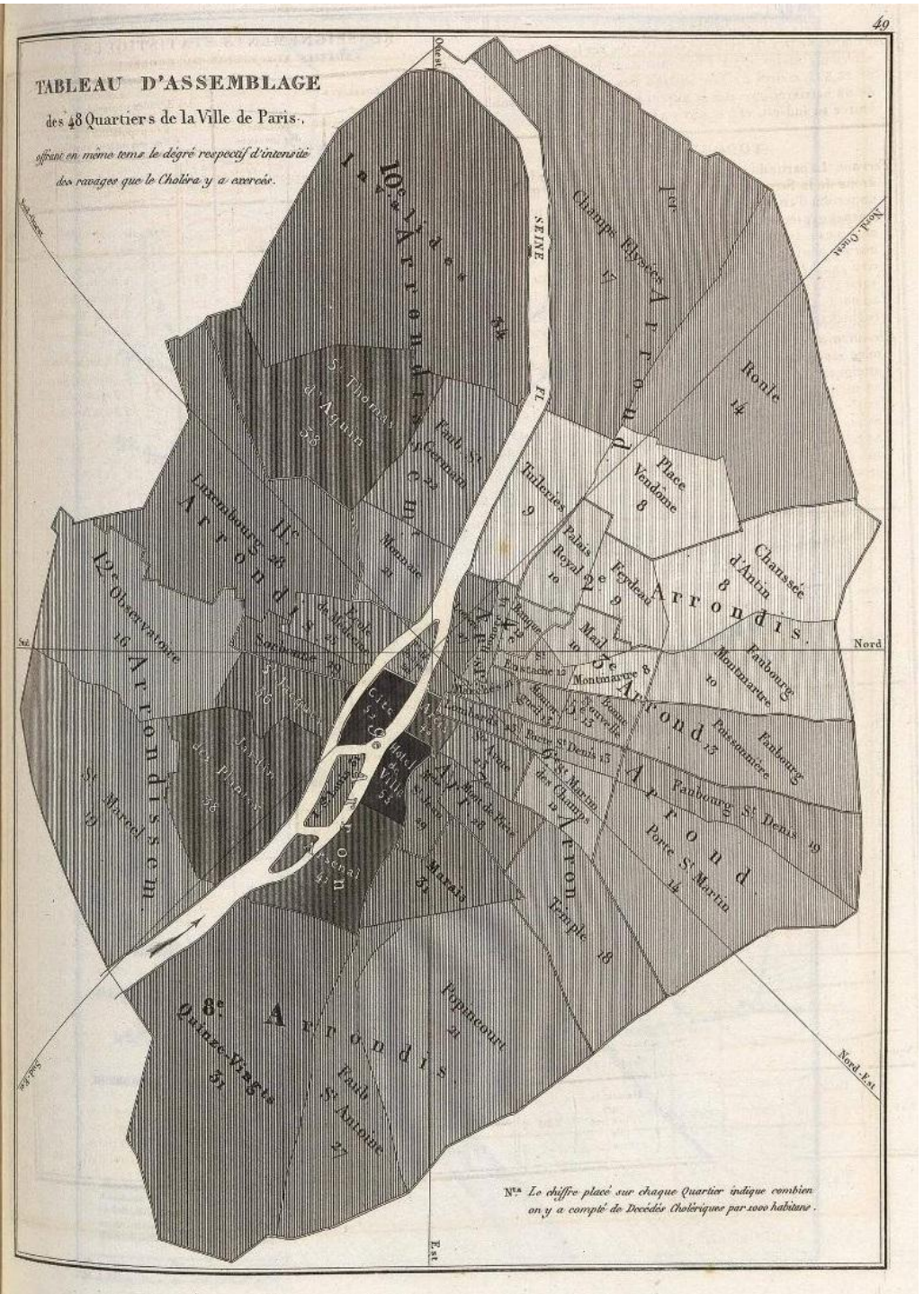
John Snow's map of cholera outbreaks from nineteenth century London changed how we saw a disease - and gave data journalists a model of how to work today

Social Science & Medicine
Volume 50, Issues 7–8, 1 April 2000, Pages 923-935

Our sense of Snow: the myth of John Snow in medical geography

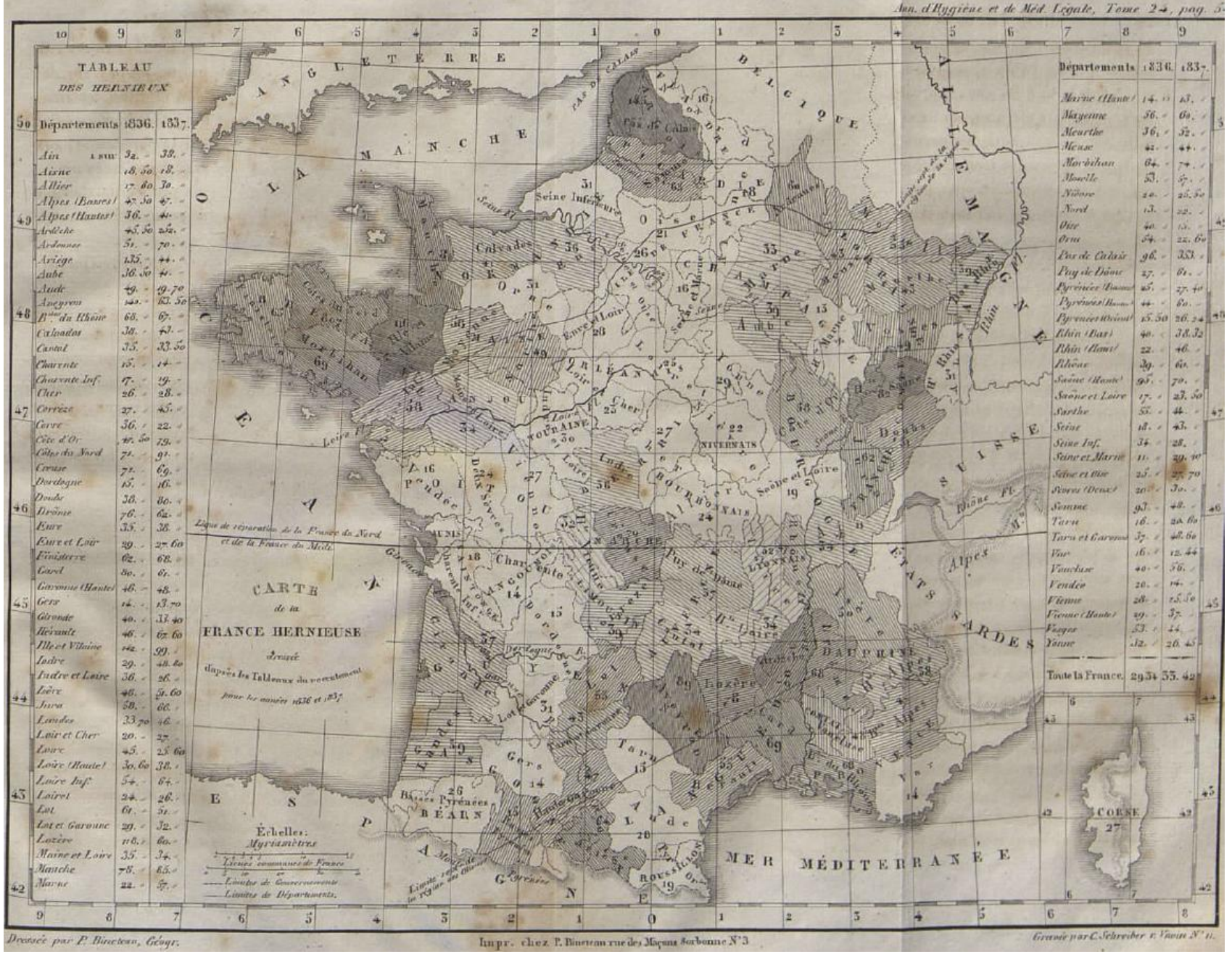


Filippo Arrieta's 1664 map of the 1660-1662 plague outbreak in the province of Bari, reproduced from



'TABLEAU D'ASSEMBLAGE des 48 Quartiers de la Ville de Paris. Offrant en même temps le degré respectif d'intensité des ravages que le Cholera y a exercés'

Charles Picquet's 1834 choroplet
map representing the mortality rates from cholera in Paris during the 1832 epidemic

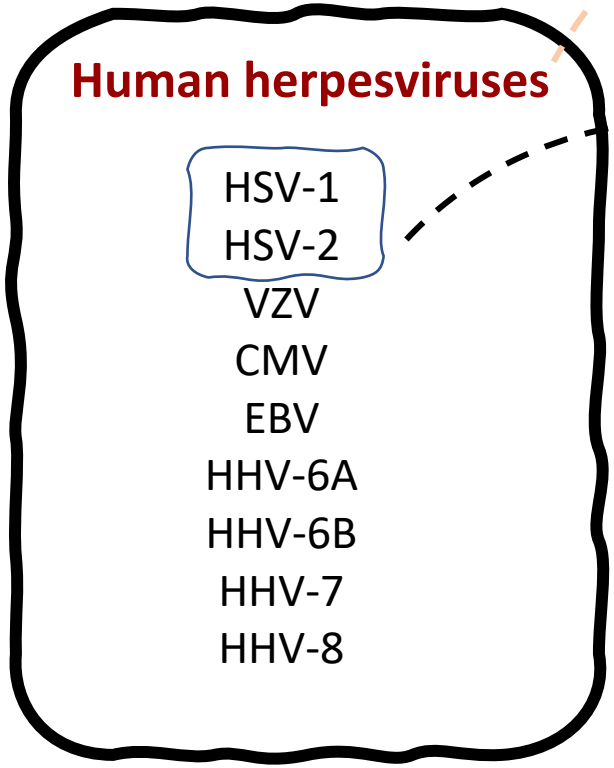


Départements	1836.	1837.
Ain	32.	38.
Aisne	18. 50	18.
Allier	17. 80	30.
Alpes (Basses)	47. 50	47.
Alpes (Hautes)	36.	41.
Ardèche	45. 50	22.
Ardennes	51.	70.
Ariège	135.	44.
Aube	38. 50	41.
Aude	49.	49. 70
Aveyron	140.	163. 50
B.es du Rhône	68.	67.
Calvados	38.	43.
Cantal	35.	33. 50
Charente	15.	14.
Charente Inf.	17.	19.
Cher	26.	28.
Corrèze	27.	45.
Corse	36.	22.
Côte d'Or	47. 50	79.
Côtes du Nord	71.	91.
Creuse	72.	69.
Dordogne	15.	16.
Doubs	38.	80.
Drôme	76.	62.
Eure	35.	36.
Eure et Loir	29.	27. 60
Finistère	62.	68.
Gard	80.	61.
Garonne (Haute)	46.	48.
Gers	14.	13. 70
Gironde	40.	33. 40
Hérault	46.	62. 60
Ille et Vilaine	142.	99.
Indre	29.	48. 80
Indre et Loire	36.	26.
Isère	46.	59. 60
Jura	58.	66.
Landes	33. 70	46.
Loir et Cher	20.	27.
Loire	45.	25. 60
Loire (Haute)	30. 60	38.
Loire Inf.	54.	64.
Loiret	24.	26.
Lot	61.	51.
Lot et Garonne	29.	32.
Lozère	116.	60.
Maine et Loire	35.	34.
Manche	78.	85.
Marne	22.	57.

Départements	1836.	1837.
Marne (Haute)	14. 50	18.
Mayenne	56.	60.
Meurthe	36.	32.
Meuse	42.	44.
Morbihan	64.	74.
Moselle	53.	57.
Nièvre	20.	25. 50
Nord	13.	22.
Oise	40.	13.
Orne	54.	22. 60
Pas de Calais	96.	353.
Puy de Dôme	27.	61.
Pyrénées (Basses)	25.	27. 40
Pyrénées (Hautes)	44.	60.
Pyrénées Orient.s	15. 50	26. 24
Rhin (Bas)	40.	38. 32
Rhin (Haut)	22.	46.
Rhône	39.	60.
Saône (Haute)	95.	70.
Saône et Loire	17.	23. 50
Sarthe	52.	44.
Seine	18.	43.
Seine Inf.	34.	28.
Seine et Marne	11.	29. 40
Seine et Oise	25.	27. 70
Sèvres (Deux)	20.	30.
Somme	93.	48.
Tarn	16.	20. 60
Tarn et Garonne	37.	48. 60
Var	16.	12. 44
Vaucluse	40.	56.
Vendée	20.	14.
Vienne	28.	15. 50
Vienne (Haute)	29.	37.
Vosges	53.	44.
Yonne	32.	20. 45
Toute la France.	29 34	35. 42

’Carte de la France Hernieuse’, Joseph-Francois Malgaigne’s map of the incidence of hernia in France in 1839

ABC OF HSVs



- Stay latent within their hosts following a primary infection
- Periodic reactivation, potentially symptomatic

Symptomatic infections
typically present with skin vesicles, and mucosal ulcerations at the inoculation site

- Responsible for GUDs known as genital herpes when inoculation site is located in anal and genital areas
- Consequences: social stigma, increased susceptibility to HIV infections

In 2020, an estimated 5.3 [3.4,7.9]% of the world population aged 15 to 49 years suffered from at least one genital herpes

Bulletin of the World Health Organization, 63 (3): 427-444 (1985)

Prevention and control of herpesvirus diseases*
Part 2. Epidemiology and immunology

A WHO MEETING[1]

RECOMMENDATIONS

At the international level, much can be done to promote the application of diagnostic methods for herpesvirus diseases, the development, control, and application of viral vaccines, and the application and control of chemotherapy, such as the following:

1. Workshops should be held to teach laboratory techniques for the production and quality control of reagents.
2. Reference reagents should be supplied to laboratories providing working reagents so that the latter may be standardized.
3. Studies should be coordinated on the evaluation of new, simple and rapid techniques and diagnostic reagents.
4. The production and quality control of reagents should be aided by the provision of relevant information to all concerned.
5. Countries should be encouraged to carry out epidemiological surveillance of herpesvirus diseases.
6. Collaborative studies should be organized to assess the impact of herpesviruses on populations living in different social and regional settings.
7. The future development of both subunit and live-virus vaccines should be aided by formulation of the requirements for the production and control of such vaccines.
8. With regard to the future application of chemotherapy and chemoprophylaxis of herpesvirus infections, an international collaborative programme should be coordinated to formulate a standardized procedure for assaying the sensitivity of herpesviruses to antiviral agents in cell culture systems. International collaborative centres should be encouraged to establish a library of selected herpesvirus mutants resistant to chemotherapeutic agents, including well-characterized laboratory virus strains with which the mutants arising from treatment of patients with herpesvirus infections can be compared.

* This article is the second of two articles based on the report of an Informal WHO Meeting on Recent Progress towards the Prevention and Control of Herpesvirus Diseases, which was held in Geneva on 14–18 November 1983. The first part was published in the last issue of the *Bulletin*, Vol. 63 (2): 185–201 (1985). A French translation of this article will appear in a later issue of the *Bulletin*. Requests for reprints should be sent to Chief, Virus Diseases, World Health Organization, 1211 Geneva 27, Switzerland.

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Bulletin of the World Health Organization, 63 (3): 427-444 (1985)

Prevention and control
Part 2. Epidemiology an

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plasmatique indétectable et de ne pas transmettre le VIH aux partenaires sexuels.

DOSSIER THÉMATIQUE MIS À JOUR LE 28 NOVEMBRE 2024

En augmentation, et plus fréquente chez les 50 ans et plus entre 2021 et 2023, la gonococcie est une infection sexuellement transmissible due au gonocoque. Cette pathologie peut avoir de lourdes conséquences.

EN SAVOIR PLUS

DOSSIER THÉMATIQUE MIS À JOUR LE 29 NOVEMBRE 2024

Les chlamydioses sont des infections sexuellement transmissibles dues à la bactérie Chlamydia Trachomatis. Limiter les contaminations passe par l'usage du préservatif et le dépistage.

EN SAVOIR PLUS

DOSSIER THÉMATIQUE MIS À JOUR LE 29 NOVEMBRE 2024

Le VIH ou Virus de l'Immunodéficience Humaine est un rétrovirus humain sexuellement transmissible. Il affaiblit le système immunitaire, et en l'absence de traitement, est responsable du sida.

EN SAVOIR PLUS

DOSSIER THÉMATIQUE MIS À JOUR LE 29 NOVEMBRE 2024

Due à la bactérie Treponema pallidum, la syphilis se transmet par voie sexuelle. Elle peut également se transmettre de la mère à l'enfant au cours de la grossesse. Cette pathologie peut affecter tous les organes et avoir de graves conséquences si elle n'est pas dépistée et traitée.

EN SAVOIR PLUS

DOSSIER THÉMATIQUE MIS À JOUR LE 17 JUIN 2019

Certains HPV infectent les muqueuses génitales. L'infection est en général asymptomatique. Dans certains cas, elle peut entrainer des lésions pouvant évoluer en cancer dont le plus fréquent est le cancer du col de l'utérus.

EN SAVOIR PLUS

DOSSIER THÉMATIQUE MIS À JOUR LE 24 SEPTEMBRE 2024

Infections virales du foie pouvant être très sévères, les hépatites B et D sont transmises par voie sexuelle, sanguine et materno-foetale.
La vaccination et le dépistage sont les piliers de la prévention.

EN SAVOIR PLUS

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Prevention and control
Part 2. Epidemiology an

MENU

3. Contribution à la surveillance épidémiologique, en lien avec l'agence nationale de santé publique

- par le recueil de données et la production de connaissances épidémiologiques en France concernant les infections à CMV chez les immunodéprimés, les infections *materno-fœtales* à Herpes virus (CMV, HSV1 et HSV2), en particulier par le recensement des infections néonatales liées aux HSV ainsi que les cas d'herpès génitaux et d'encéphalite herpétique ;

?????? ?????? ??????

- par le suivi de la résistance aux antiviraux des souches isolées chez les immunodéprimés (transplantés et receveurs de cellules souches hématopoïétiques, lymphomes, etc.) ;
- en participant au réseau de surveillance européen des génotypes et des résistances aux antiviraux.

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This study aims to improve our epidemiological knowledge of the contribution of HSV-1 and HSV-2 to GUDs and its potential spatial heterogeneity

DATA

HSV-1 and HSV-2 PCR results on GUD (binary results)

GUDs sampled between 1 January 2022 and 30 December 2024

Limited data available:

- Sex
- Age
- District of residence

DESCRIPTIVE STATISTICS

N GUDs

34,740

N (%) Positive HSV-1

6,539 (18.82%)

N (%) Positive HSV-2

4,833 (13.91%)

N (%) Positive HSV-1 AND HSV-2

31 (<0.1%)

So small that we did not bother to explicitly handle such a case.

% PCR positive HSV-2 among all positive PCRs

42.5%

SPATIAL DATA, SMALL-AREA ESTIMATION PROBLEM, SMOOTHING

Everything is related to everything else, but near things are more related than distant things.

Tobler's First Law of Geography, Waldo Tobler

Spatiotemporal data are non-exchangeable

Spatiotemporal data are autocorrelated across space and time

Sampling sparse in space:

prevent the computation of metrics of interest or yield large and unstable uncertainty intervals

Bayesian hierarchical models with multivariate priors

Gaussian Markov Random Fields

$x = (x_1, \dots, x_n)$ is a GMRF with respect to an undirected labelled graph $\mathcal{G}$ with expectation μ and a positive definite precision matrix Q, if and only if the conditional density of x takes the following form:

$$\pi_x\left(x \mid (\mu, Q)\right) = (2\pi)^{-n/2} \mid Q \mid^{1/2} \exp\left(-\frac{1}{2}(x-\mu)' Q (x-\mu)\right)$$

- Simply a multivariate distribution parametrised through its precision matrix Q (inverse of the covariance matrix)
- Q encode the conditional dependence between the elements of x

$$\begin{cases} \mathbb{E}(x_i \mid \underbrace{\{x_j,\ j \neq i\}}_{x_{-i}}) = \mu_i - \frac{1}{Q_{ii}} \sum_{j:j\neq i} Q_{ij}(x_j - \mu_j) \\ \mathbb{P}(x_i \mid x_{-i}) = \mathbb{V}(x_i \mid x_{-i})^{-1} = Q_{ii} \\ \mathbb{C}(x_i, x_j \mid \underbrace{\{x_k,\ k \neq i \text{ and } k \neq j\}}_{x_{-ij}}) = -\frac{Q_{ij}}{\sqrt{Q_{ii}Q_{jj}}} \end{cases}$$

- **Basic tools for spatial, temporal, spatiotemporal modelling**
- **'New-style random-effect': COMPONENT OF THE MEAN, NOT OF THE VARIANCE**

SOME EXAMPLE

Routinely used temporal GMRF

AR(1) process, $Q = \tau R_{AR(1)}(\rho)$

$$R_{\mathrm{AR}(1)}(\rho) = \begin{pmatrix} 1 & -\rho & 0 & \dots & 0 \\ -\rho & 1+\rho^2 & -\rho & \dots & 0 \\ 0 & -\rho & 1+\rho^2 & \ddots & \vdots \\ \vdots & \vdots & \ddots & \ddots & -\rho \\ 0 & 0 & \dots & -\rho & 1 \end{pmatrix}$$

RW(1) process, $Q = \tau R_{RW(1)}$

$$R_{RW(1)} = \begin{pmatrix} 1 & -1 & 0 & 0 & \dots & 0 & 0 \\ -1 & 2 & -1 & 0 & \dots & 0 & 0 \\ 0 & -1 & 2 & -1 & \dots & 0 & 0 \\ 0 & 0 & -1 & 2 & \ddots & \vdots & \vdots \\ \vdots & \vdots & \vdots & \ddots & \ddots & -1 & 0 \\ 0 & 0 & 0 & \dots & -1 & 2 & -1 \\ 0 & 0 & 0 & \dots & 0 & -1 & 1 \end{pmatrix}$$

RW(2) process, $Q = \tau R_{RW(2)}$

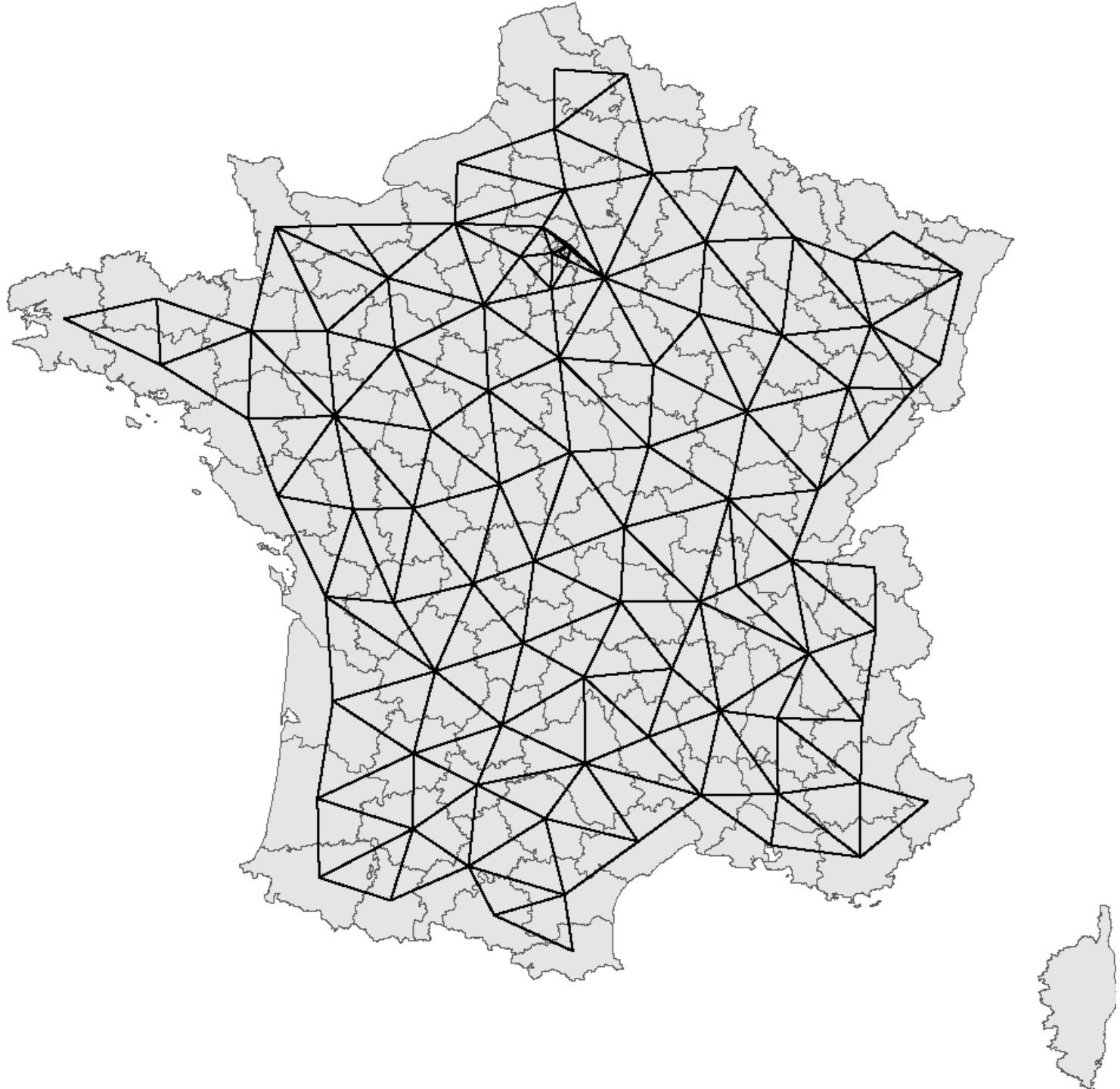
$$R_{RW(2)} = \begin{pmatrix} 1 & -2 & 1 & 0 & 0 & \dots & 0 & 0 \\ -2 & 5 & -4 & 1 & 0 & \dots & 0 & 0 \\ 1 & -4 & 6 & -4 & 1 & \dots & 0 & 0 \\ 0 & 1 & -4 & 6 & -4 & \ddots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & 1 & -4 & 6 & -4 & 1 \\ 0 & 0 & \dots & 0 & 1 & -4 & 5 & -2 \\ 0 & 0 & \dots & 0 & 0 & 1 & -2 & 1 \end{pmatrix}$$

Routinely used spatial GMRF (BYM2)

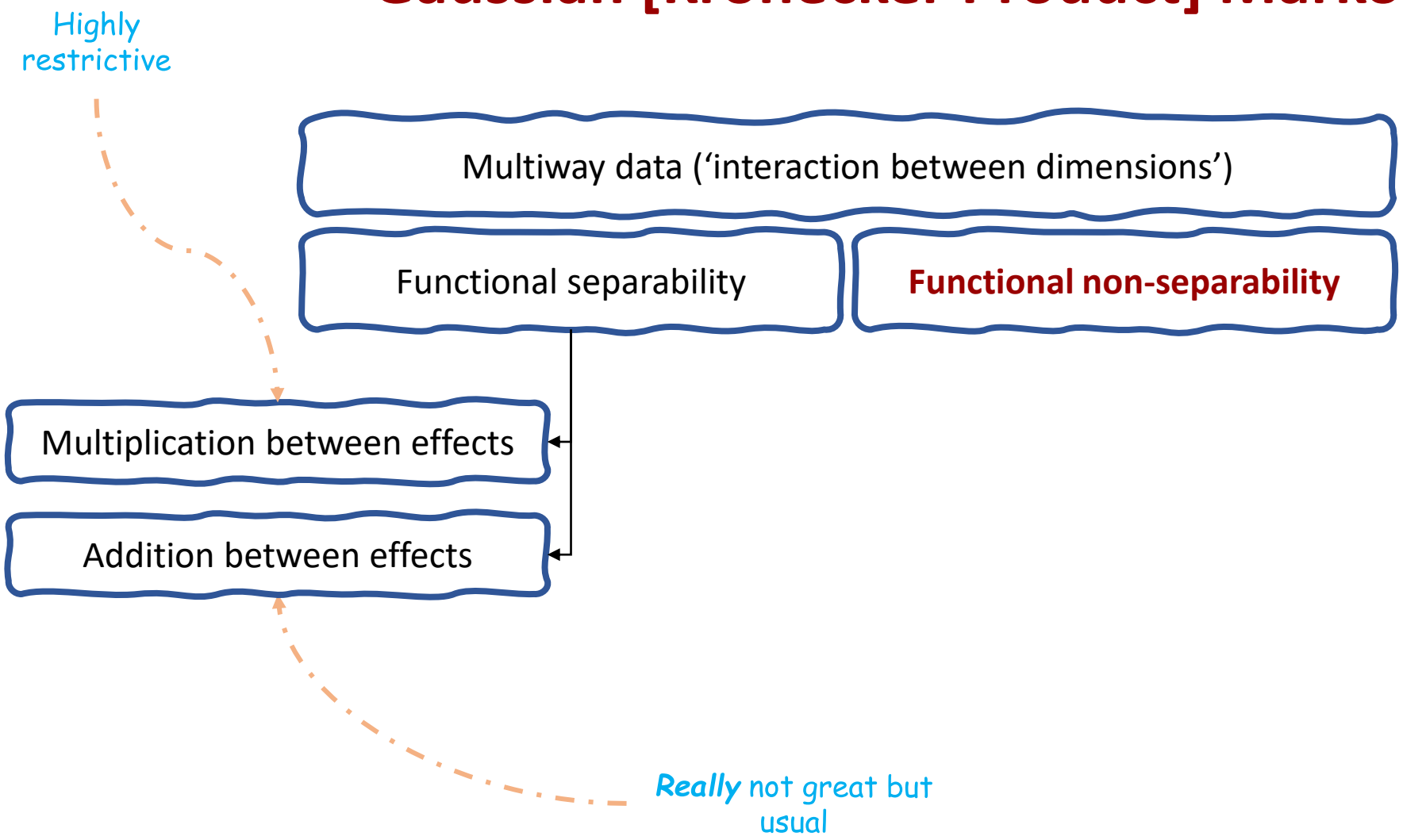
$$\begin{cases} x = \frac{1}{\sqrt{\tau}}\left(\sqrt{(1-\phi)}v + \sqrt{\phi}u\right) \\ u \sim \mathcal{N}(0, R_*^-) \\ v \sim \mathcal{N}(0, I) \\ R_* : \text{Scaled } R \\ R = D - W \end{cases}$$

$$R = \bar{s}R_*, \bar{s} = \exp\left(\frac{1}{n}\sum_i (R^-)_{ii}\right)$$

$$Q = \begin{pmatrix} \frac{\tau}{1-\phi}I & -\frac{(\phi\tau)^{1/2}}{1-\phi}I \\ -\frac{(\phi\tau)^{1/2}}{1-\phi}I & R_* + \frac{\phi}{1-\phi}I \end{pmatrix}$$



Gaussian [Kronecker Product] Markov Random Fields



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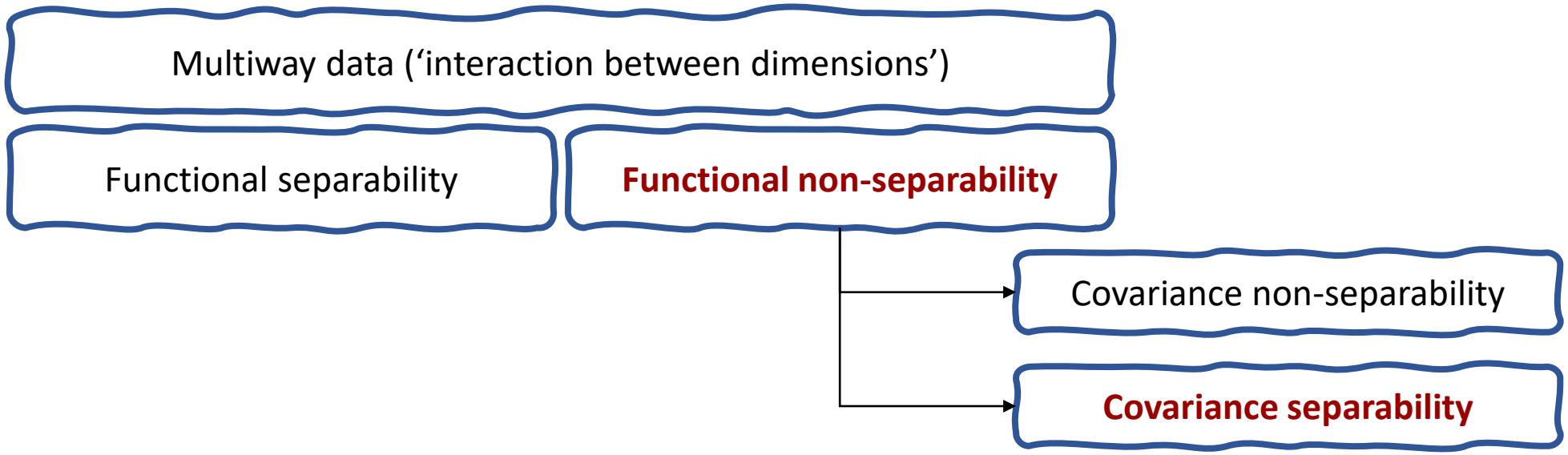
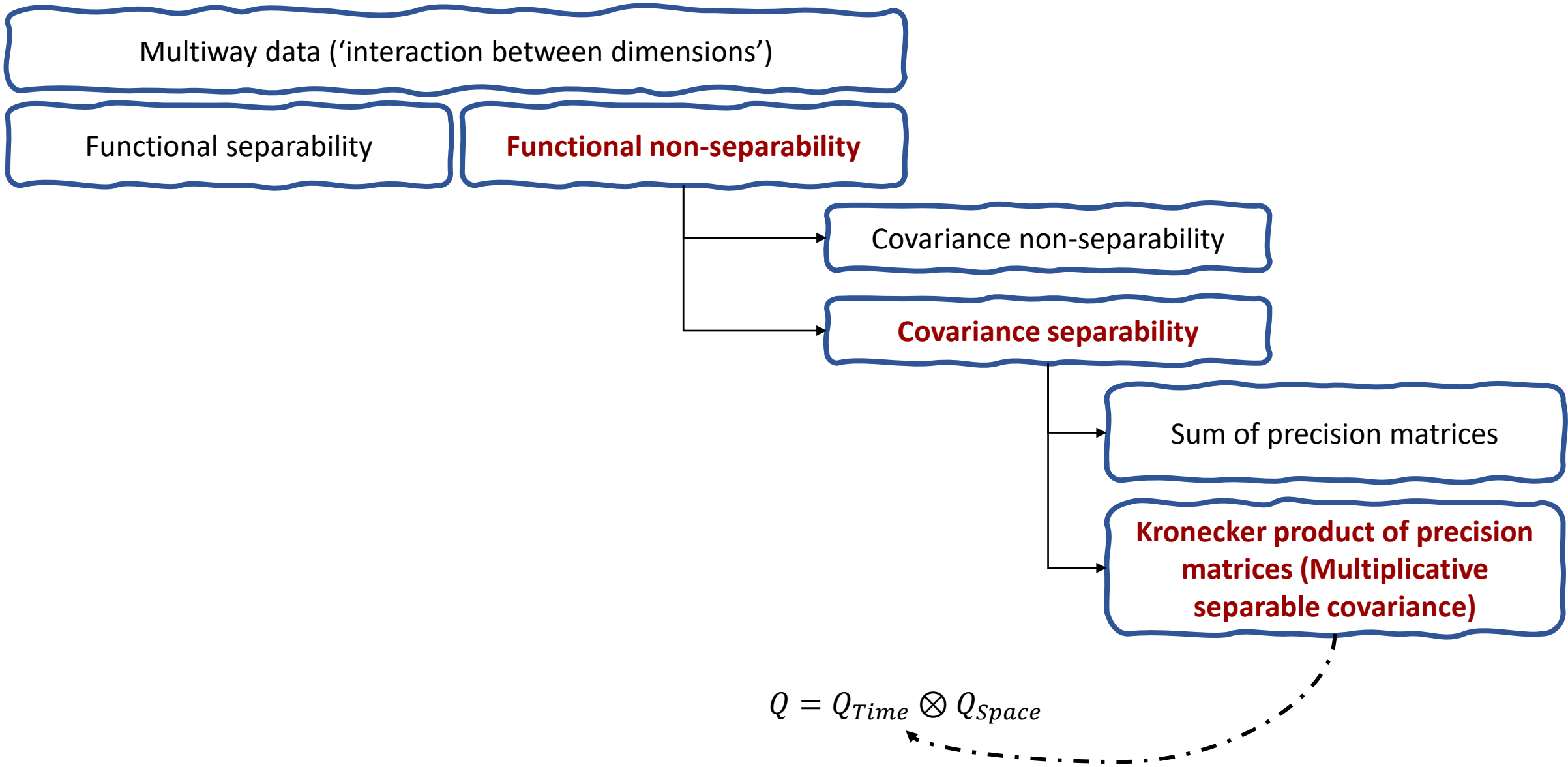


Gaussian [Kronecker Product] Markov Random Fields



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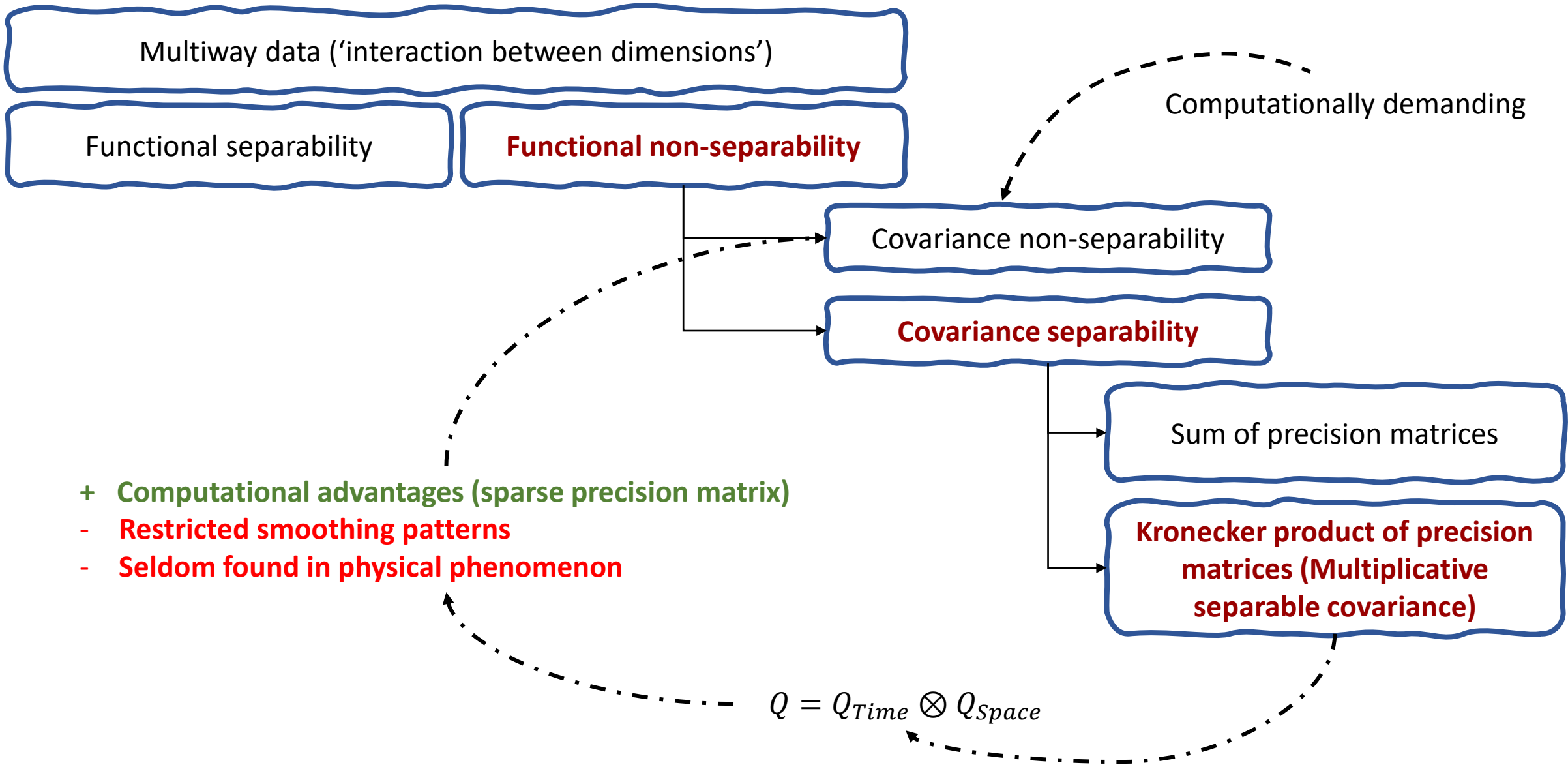


Gaussian Random Fields (GRF)

A Gaussian Random Fields $x(s), s \in \mathbb{R}^d$, is a stochastic process such that:

- $\mathbb{E}[x(s)] = m(s)$
- $\mathbb{C}\big(x(s), x(s')\big) = c(s, s')$
- $(x(s_1), \dots, x(s_n)) \sim \mathcal{N}\left(\left(m(s_i)\right)_{i\in\{1,\dots,n\}}, \left(c\left(s_i, s_j\right)\right)_{(i,j)\in\{1,\dots,n\}^2}\right)$

Usual choice in geostatistics: Matérn covariance function

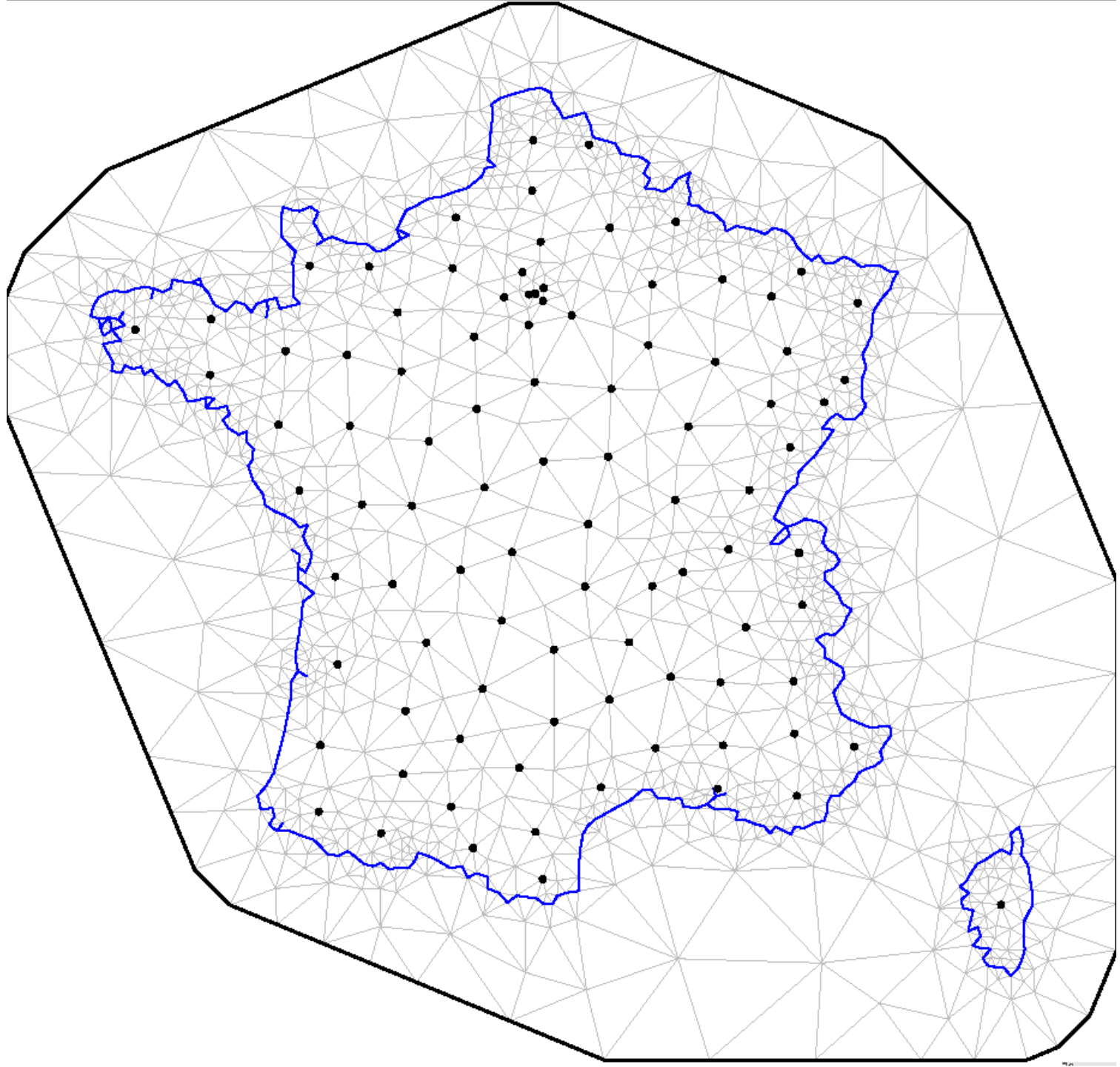
$$c(s_1, s_2) = \frac{\sigma^2}{2^{\nu-1}\mathrm{T}(\nu)} \kappa d(s_1, s_2) K_\nu(\kappa d(s_1, s_2))$$

In this classical form: Isotropic and stationary

Scale badly, cost of $\mathcal{O}(N^3)$

Classical solution since Lindgren et al. 2011: GMRF approximation

cost of $\mathcal{O}\left(n^{3/2}\right)$

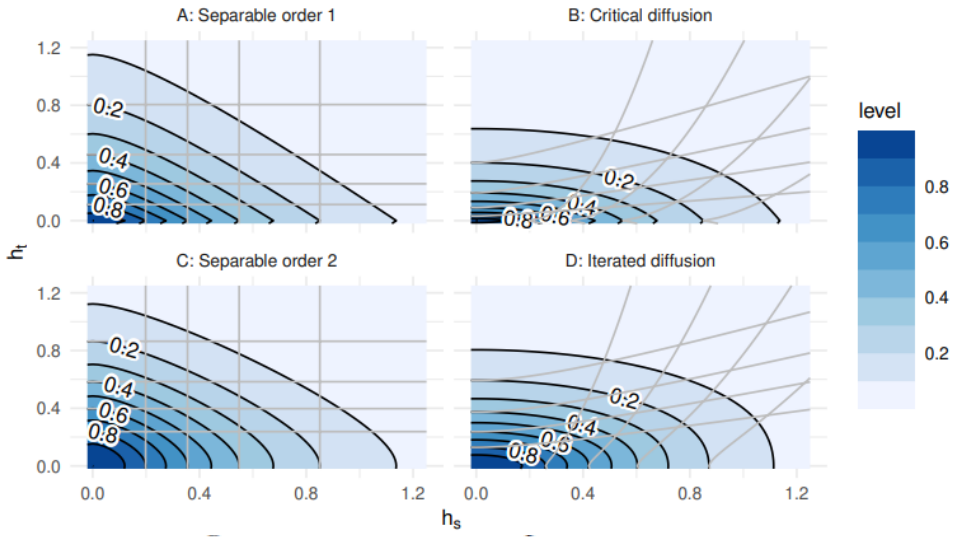


Diffusion extension of the Matérn fields (DEMF)

Lindgren et al. (2024) introduce a class of spatiotemporal GRF inspired by diffusion processes

$$
\begin{cases}
\alpha = \alpha_e + \alpha_s(\alpha_t - 1/2) \\
\nu_s = \alpha - d/2 > 0 \\
\nu_t > 0 \\
R_\nu^M(t) = \frac{1}{\Gamma(\nu)2^{\nu-1}} t^\nu K_\nu(t),\ t \geq 0 \\
C_{\mathbb{R}^d,\alpha} = \frac{\Gamma(\alpha - d/2)}{\Gamma(\alpha)(4\pi)^{d/2}} \\
\sigma^2 = \frac{C_{\mathbb{R},\alpha_t} C_{\mathbb{R}^d,\alpha}}{\gamma_e^2 \gamma_t \gamma_s^{2\alpha-d}} \\
C_{\alpha_t,\alpha_s,\alpha_e,\gamma_t,\gamma_s,\gamma_e}(x(s,t), x(s',t)) = \sigma^2 R_{\nu_s}^M(\gamma_s d(s,s'))
\end{cases}
$$

- Marginal spatial covariance: Matérn function
- Marginal temporal: no closed form
- Separability of the process can be controlled through a single parameter



Model	α_t	α_s	α_e	Type	ν_t	ν_s
$DEMF(1,0,2)$	1	0	2	Separable order 1	1/2	1
$DEMF(1,2,1)$	1	2	1	Critical diffusion	1/2	1
$DEMF(2,0,2)$	2	0	2	Separable order 2	3/2	1
$DEMF(2,2,0)$	2	2	0	Iterated diffusion	1	2

For four specific cases, they produced GMRF approximation of this process

BASELINE MODEL - BINOMIAL LIKELIHOOD

$$y_{v,a,s,t,d} | N_{a,s,t,d}, p_{v,a,s,t,d} \sim Bin(N_{a,s,t,d}, p_{v,a,s,t,d})$$

$$p_{v,a,s,t,d} = \mathrm{g}^{-1}(\mu_{v,s,a,t,d}) \in (0,1)$$

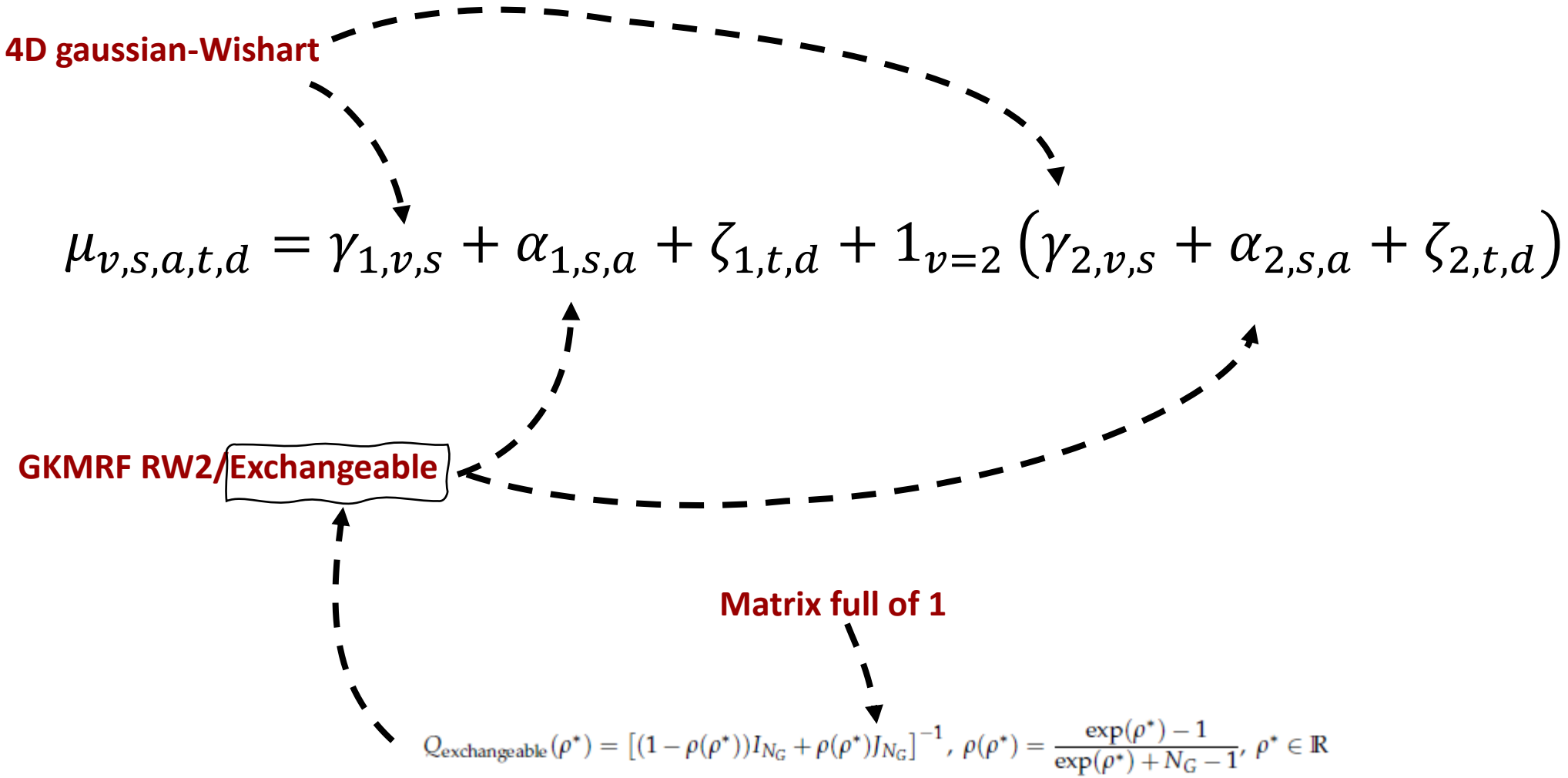
$$\mu_{v,s,a,t,d} = \gamma_{1,v,s} + \alpha_{1,s,a} + \zeta_{1,t,d} + 1_{v=2}\left(\gamma_{2,v,s} + \alpha_{2,s,a} + \zeta_{2,t,d}\right) \in (-\infty, +\infty)$$

BASELINE MODEL - BINOMIAL LIKELIHOOD

4D gaussian-Wishart

$$\mu_{v,s,a,t,d} = \gamma_{1,v,s} + \alpha_{1,s,a} + \zeta_{1,t,d} + 1_{v=2}\left(\gamma_{2,v,s} + \alpha_{2,s,a} + \zeta_{2,t,d}\right)$$

BASELINE MODEL - BINOMIAL LIKELIHOOD



BASELINE MODEL - BINOMIAL LIKELIHOOD

4D gaussian-Wishart

$$\mu_{v,s,a,t,d} = \gamma_{1,v,s} + \alpha_{1,s,a} + \zeta_{1,t,d} + 1_{v=2}\left(\gamma_{2,v,s} + \alpha_{2,s,a} + \zeta_{2,t,d}\right)$$

GKMRF RW2/Exchangeable

(hyperparameters different for α_1 and α_2)

'You are only one decision away from a totally different (certainly better) life'

BASELINE MODEL - BINOMIAL LIKELIHOOD

		Link function
		Logit
Spatiotemporal prior (same type but different hyperparameters for ζ_1 and ζ_2)	**DEMF(102)**	X
	DEMF(220)	X
	DEMF(202)	X
	DEMF(121)	X
	BYM2-RW(2)	X
	BYM2-RW(1)	X
	BYM2-AR(1)	X

Remember our friend the link function?

If you don't like this one, I've got others

		Link function								
		Logit	Cauchit	Probit	Cloglog	Powerlogit	Robit 3	Robit 4	Robit 5	Robit 6
Spatiotemporal prior	DEMF(102)	X								
	DEMF(220)	X								
	DEMF(202)	X								
	DEMF(121)	X								
	BYM2-RW(2)	X								
	BYM2-RW(1)	X								
	BYM2-AR(1)	X	X	X	X	X	X	X	X	X

A last ride towards computational hell

		Link function								
		Logit	Cauchit	Probit	Cloglog	Powerlogit	Robit 3	Robit 4	Robit 5	Robit 6
Spatiotemporal prior	DEMF(102)	X								
	DEMF(220)	X								
	DEMF(202)	X								
	DEMF(121)	X								
	BYM2-RW(2)	X								
	BYM2-RW(1)	X								
	BYM2-AR(1)	X	X	X	X	X	X	X	X	X
Preferential sampling (1)							X			
Preferential sampling (2)							X			

They look like that

ZOOM ON THE PREFERENTIAL SAMPLING MODEL

Truncated Poisson

$$N_{a,s,t,d} | p_{1,a,s,t,d}, p_{2,a,s,t,d} \sim nzPois(\lambda_{a,s,t,d})$$

$$\varepsilon\left(-\frac{\log(0.01)}{0.7}\right)$$

$$\lambda_{a,s,t,d} = \log(\lambda^*_{a,s,t,d})$$

Beta(1,1)

$$(1)\lambda^*_{a,s,t,d} = \zeta_{v,s} + \beta_{s,a} + \xi_{t,d} + \theta(w.p_{1,a,s,t,d} + (1-w).p_{2,a,s,t,d})$$

$$(2)\lambda^*_{a,s,t,d} = \zeta_{v,s} + \beta_{s,a} + \xi_{t,d} + \exp(\theta^*_s)\,(w.p_{1,a,s,t,d} + (1-w).p_{2,a,s,t,d})$$

2D gaussian-Wishart

2D gaussian-Wishart

Model structure uncertainty and probably none of them is the 'true model' (☹)

M-CLOSED, M-COMPLETE, M-OPEN

Following Bernardo and Smith

M-closed

- The true model is unknown
- Thanks to the analyst's magical powers, the true model belongs to the set of candidate models M

M-complete

- The true model is unknown
- Stakeholders routinely act as if a Bayesian belief model M^* were the true model
- This model M^* is too burdensome for a regular use
- M contains surrogate model to overcome this limitation

M-open

- The true model is unknown
- No Bayesian belief model M^* is available
- The goal of the analysis is to produce a potential Bayesian belief model candidate
- Such a model must have good generalisability properties

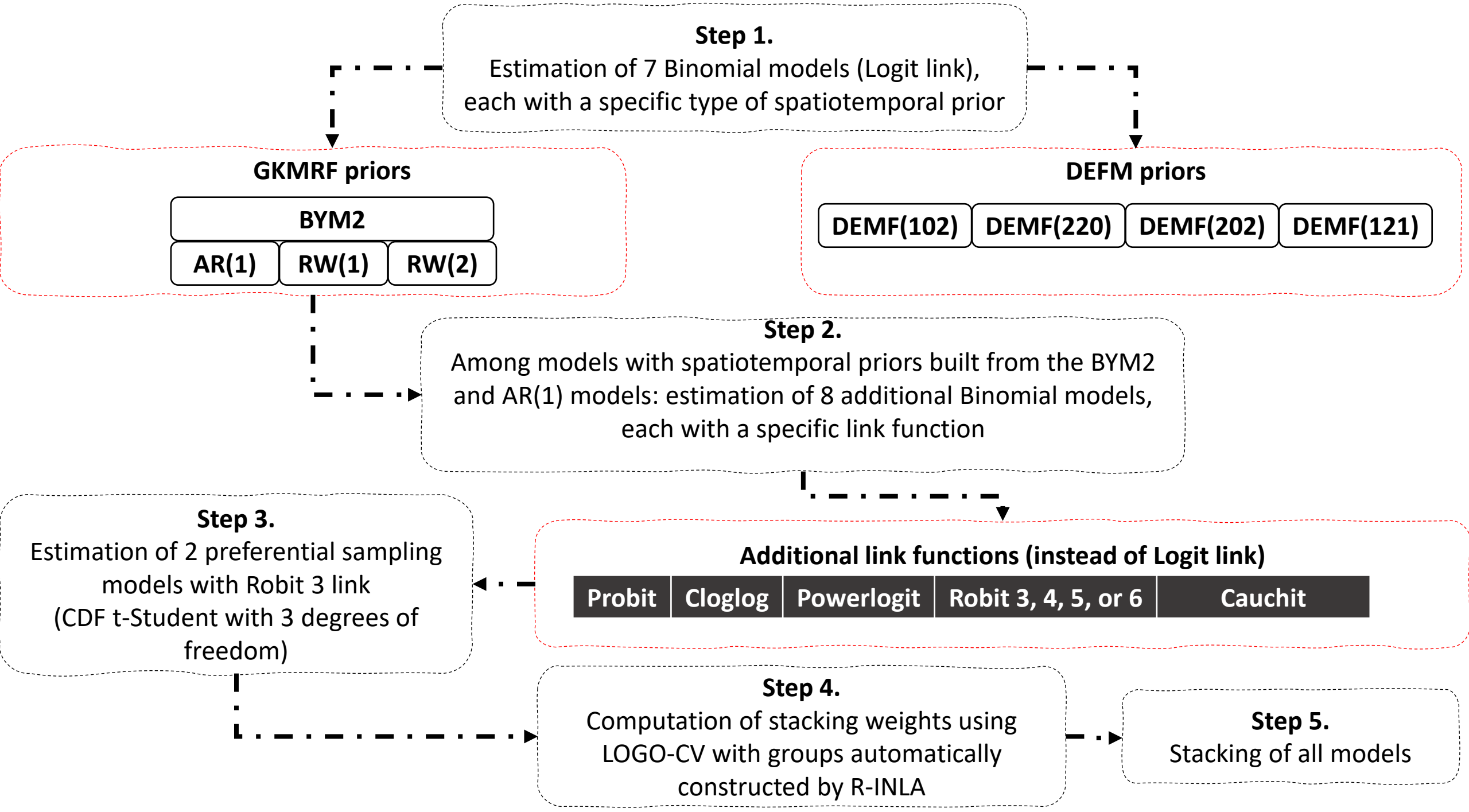
BAYESIAN STACKING: BMA IN THE M-OPEN WORLD

$$p(\Delta|y) = \sum_{M \in \mathcal{M}} w_M^* p(\Delta|y, M)$$

Log-score
- Local
- Strictly proper

LO(G)O-CV

$$w^* = \arg\min_{w_M} - \sum_{i=1}^{N} \log\left(\sum_{M \in \mathcal{M}} w_M p\left(y_i \middle| y_{-\mathcal{G}(i|M)}, M\right)\right)$$


Step 1.
Estimation of 7 Binomial models (Logit link), each with a specific type of spatiotemporal prior
GKMRF priors
BYM2
AR(1)
RW(1)
RW(2)
DEFM priors
DEMF(102)
DEMF(220)
DEMF(202)
DEMF(121)
Step 2.
Among models with spatiotemporal priors built from the BYM2 and AR(1) models: estimation of 8 additional Binomial models, each with a specific link function
Additional link functions (instead of Logit link)
Probit
Cloglog
Powerlogit
Robit 3, 4, 5, or 6
Cauchit
Step 3.
Estimation of 2 preferential sampling models with Robit 3 link (CDF t-Student with 3 degrees of freedom)
Step 4.
Computation of stacking weights using LOGO-CV with groups automatically constructed by R-INLA
Step 5.
Stacking of all models

MODEL ASSESSMENT AND WEIGHTS

Model			Metrics							Rank						
Prior structure			LOGO-CV(k)							LOGO-CV(k)						
Type	Prior	Link	(1)	(5)	(10)	(15)	(20)	(25)	(30)	(1)	(5)	(10)	(15)	(20)	(25)	(30)
Regular model	AR(1)	Robit(3)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	3	5	5	1	2	2	4
Preferential sampling (2)	AR(1)	Robit(3)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	1	1	1	2	1	1	2
Preferential sampling (1)	AR(1)	Robit(3)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	2	2	2	3	3	3	1
Regular model	AR(1)	Cloglog	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	4	3	3	4	5	4	5
Regular model	AR(1)	Robit(4)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	5	4	4	5	4	5	3
Regular model	AR(1)	Robit(5)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	6	6	6	6	6	6	6
Regular model	DEMF(102)	Logit	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	8	9	8	7	8	9	8
Regular model	AR(1)	Robit(6)	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	7	7	7	8	7	7	7
Regular model	DEMF(202)	Logit	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	10	10	10	9	10	10	10
Regular model	AR(1)	Logit	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	0.4453	9	8	9	10	9	8	9
Regular model	AR(1)	Probit	0.4454	0.4454	0.4454	0.4454	0.4454	0.4454	0.4454	12	11	11	11	11	11	11
Regular model	AR(1)	Powerlogit	0.4454	0.4454	0.4454	0.4454	0.4454	0.4454	0.4454	14	13	12	12	12	12	12
Regular model	DEMF(220)	Logit	0.4454	0.4454	0.4454	0.4454	0.4455	0.4455	0.4455	13	14	14	13	14	14	14
Regular model	DEMF(121)	Logit	0.4454	0.4454	0.4454	0.4454	0.4454	0.4455	0.4455	11	12	13	14	13	13	13
Regular model	AR(1)	Cauchit	0.4455	0.4455	0.4455	0.4455	0.4455	0.4455	0.4456	15	15	15	15	15	15	15
Regular model	RW(1)	Logit	0.4461	0.4461	0.4461	0.4461	0.4461	0.4462	0.4462	16	16	16	16	16	16	16
Regular model	RW(2)	Logit	0.4475	0.4475	0.4475	0.4475	0.4475	0.4475	0.4475	17	17	17	17	17	17	17

Link	Prior	Weights	Draws (1)	Draws (2)
Cloglog	AR(1)	0.14851	743	446
Powerlogit	AR(1)	0.10891	545	327
Logit	AR(1)	0.09901	495	297
Robit(5)	AR(1)	0.09901	495	297
Logit	DEMF(202)	0.08911	446	267
Probit	AR(1)	0.07921	396	238
Robit(4)	AR(1)	0.07921	396	238
Robit(6)	AR(1)	0.07921	396	238
Logit	DEMF(220)	0.06931	347	208
Logit	RW(1)	0.06931	347	208
Logit	RW(2)	0.04950	248	149
Logit	DEMF(102)	0.02970	149	89
Logit	DEMF(121)	0.00000	0	0
Cauchit	AR(1)	0.00000	0	0
Robit(3)	AR(1)	0.00000	0	0
Robit(3) - Preferential sampling (1)	AR(1)	0.00000	0	0
Robit(3) - Preferential sampling (2)	AR(1)	0.00000	0	0

CONDITIONAL vs. MARGINAL

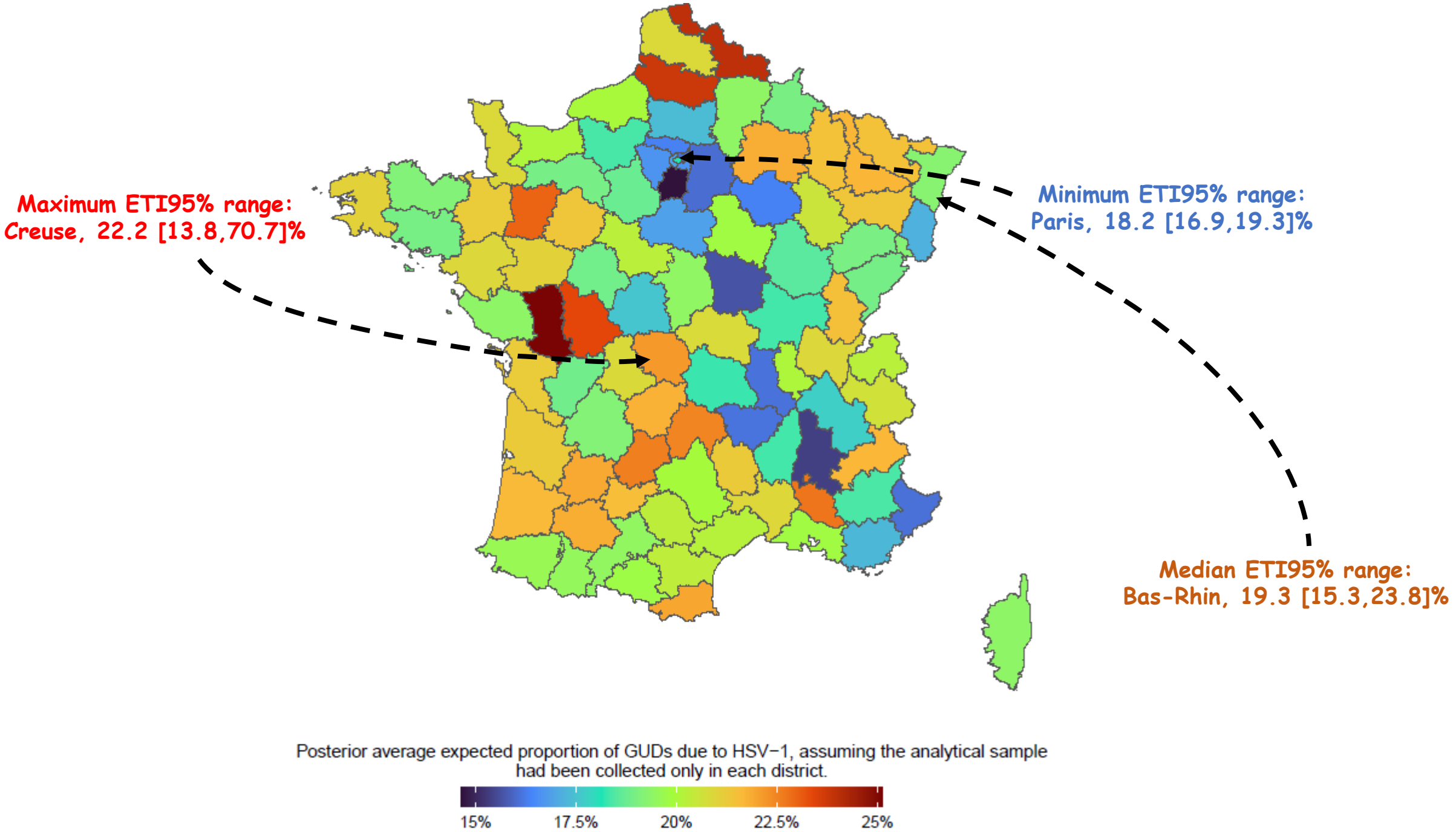
- The **binomial model** provides a **conditional expected proportion** of success for a given set of covariates

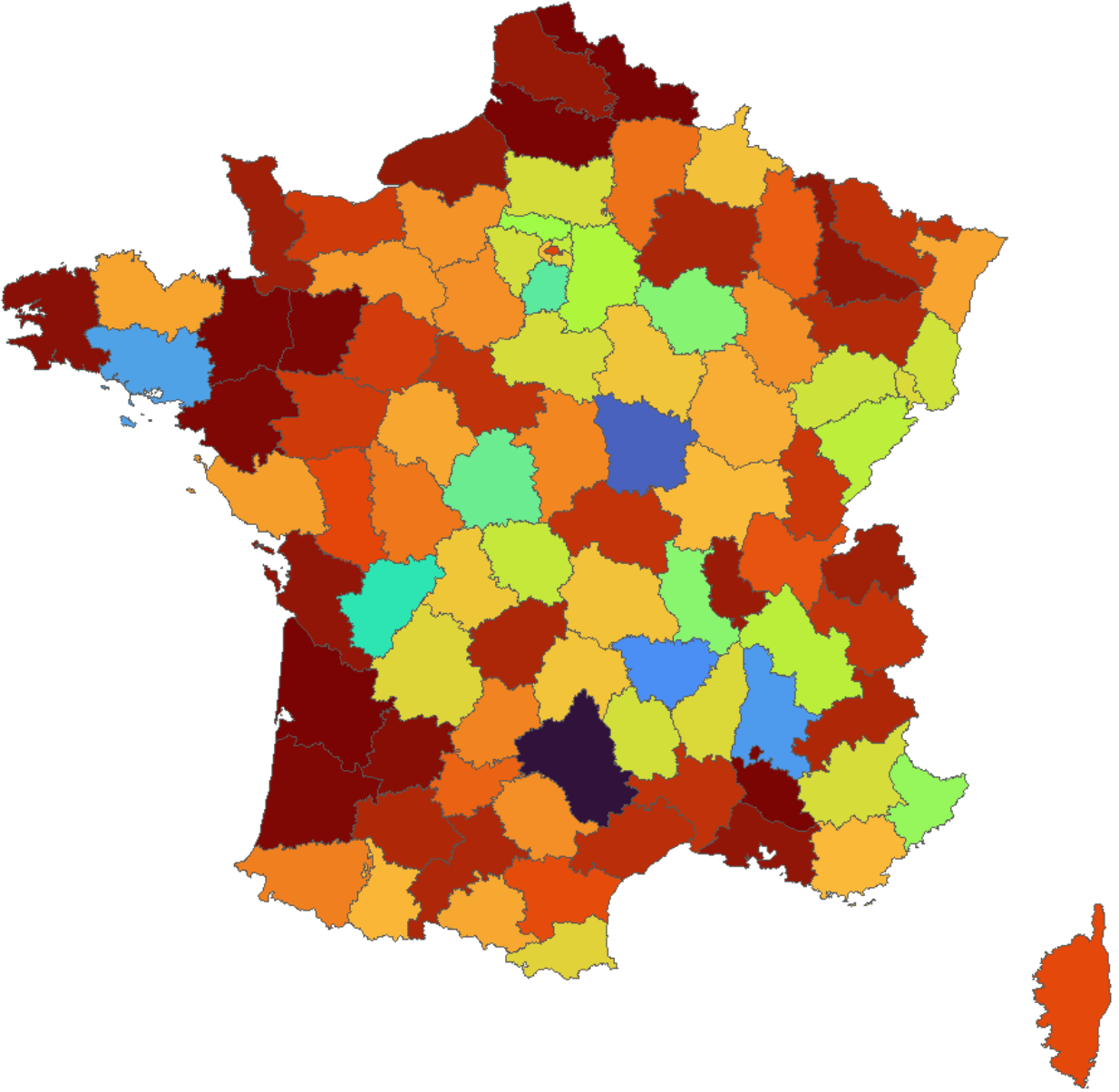
$$\underbrace{2}_{\text{sex}} \times \underbrace{156}_{\text{time}} \times \underbrace{95}_{\text{space}} \times \underbrace{101}_{\text{age}} = 2{,}993{,}640$$

This is unknown

- Proper marginalisation requires the correct distribution for N in the target population

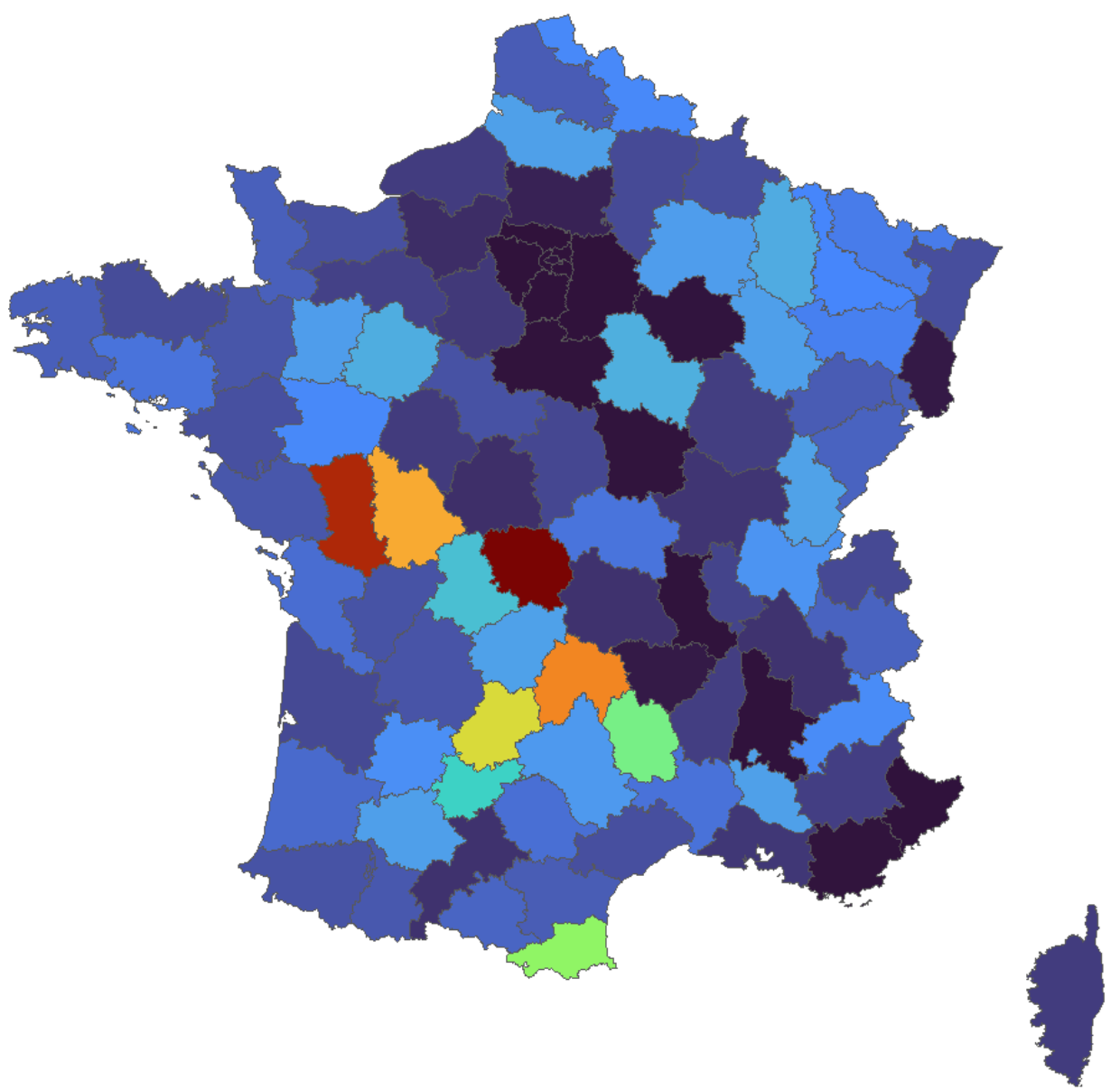
Fallback solution: 'dummy marginalisation' using the insample distribution of N


Maximum ETI95% range:
Creuse, 22.2 [13.8,70.7]%
Minimum ETI95% range:
Paris, 18.2 [16.9,19.3]%
Median ETI95% range:
Bas-Rhin, 19.3 [15.3,23.8]%
Posterior average expected proportion of GUDs due to HSV−1, assuming the analytical sample had been collected only in each district.
15%
17.5%
20%
22.5%
25%



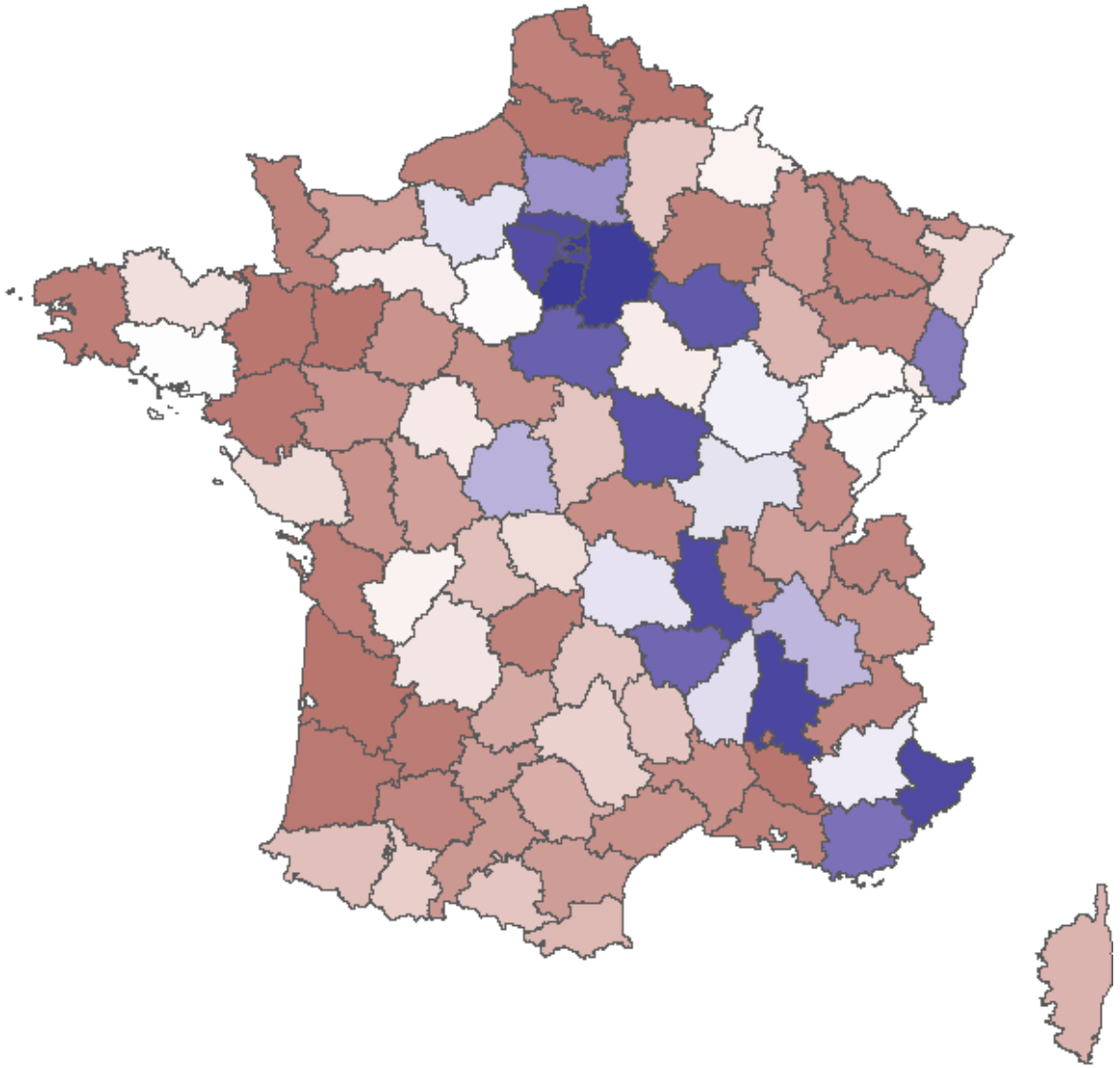
Posterior LB ETI95% expected proportion of GUDs due to HSV-1, assuming the analytical sample had been collected only in each district.

10% 12.5% 15% 17.5%



Posterior UB ETI95% expected proportion of GUDs due to HSV-1, assuming the analytical sample had been collected only in each district.

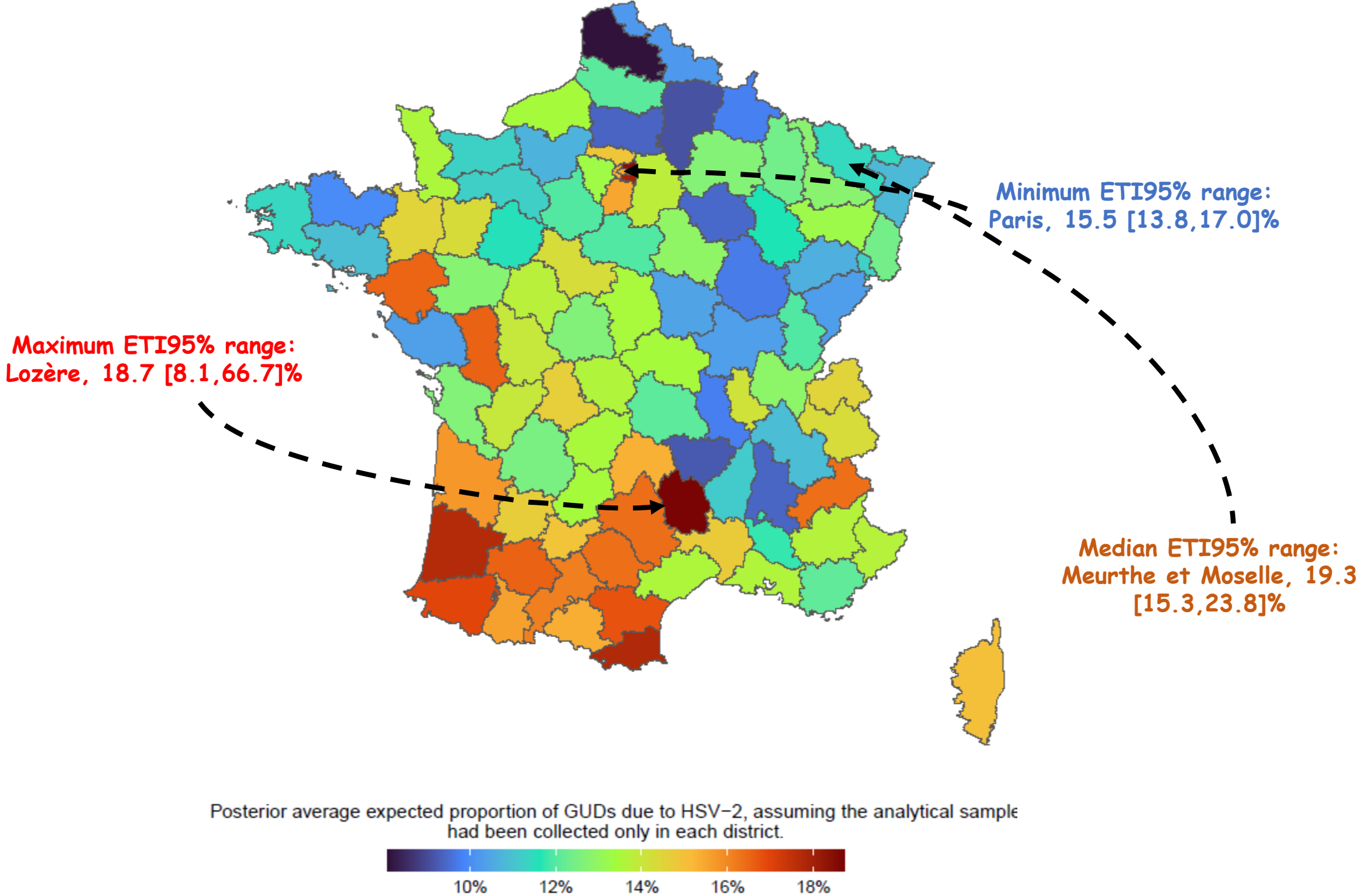
20% 30% 40% 50% 60% 70%

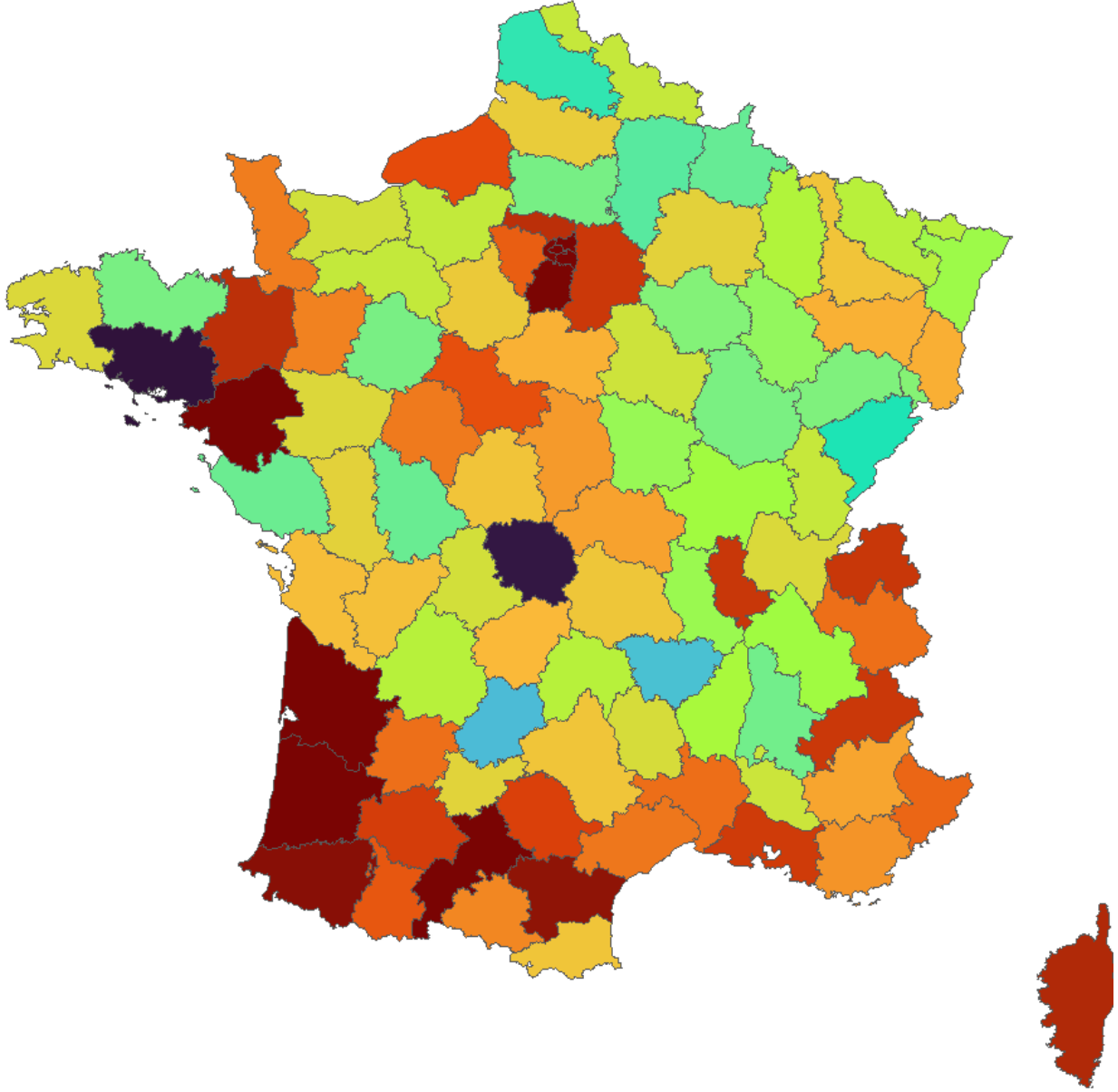


Posterior probability of positive difference in expected proportion of GUDs due to HSV−1, assuming the analytical sample had been collected only in each district compared with only collected in Paris.

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

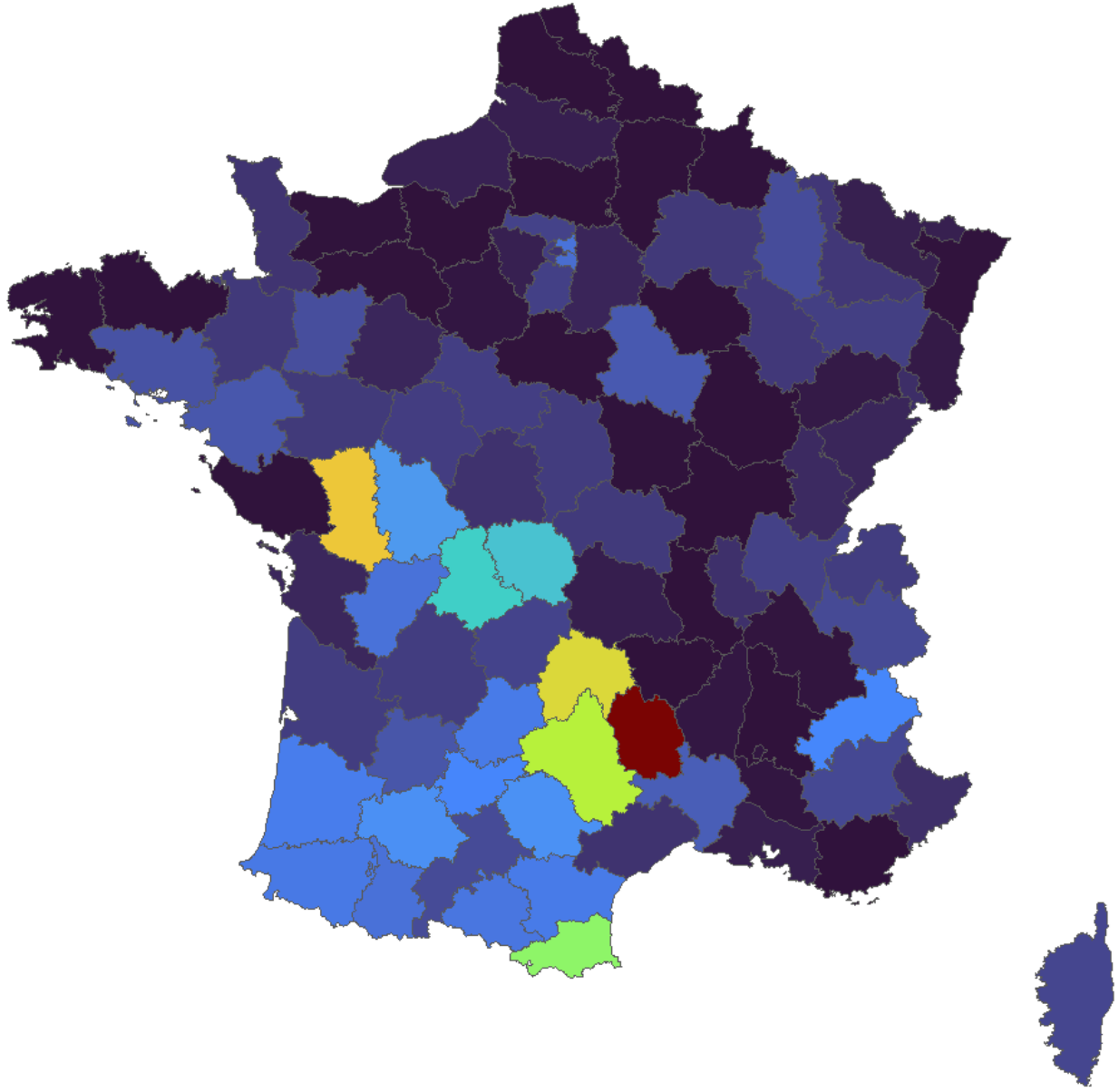
Probability threshold	Number of districts with probability > threshold
0.5	68
0.8	8
0.9	0


Minimum ETI95% range:
Paris, 15.5 [13.8,17.0]%
Maximum ETI95% range:
Lozère, 18.7 [8.1,66.7]%
Median ETI95% range:
Meurthe et Moselle, 19.3
[15.3,23.8]%
Posterior average expected proportion of GUDs due to HSV−2, assuming the analytical sample had been collected only in each district.
10%
12%
14%
16%
18%



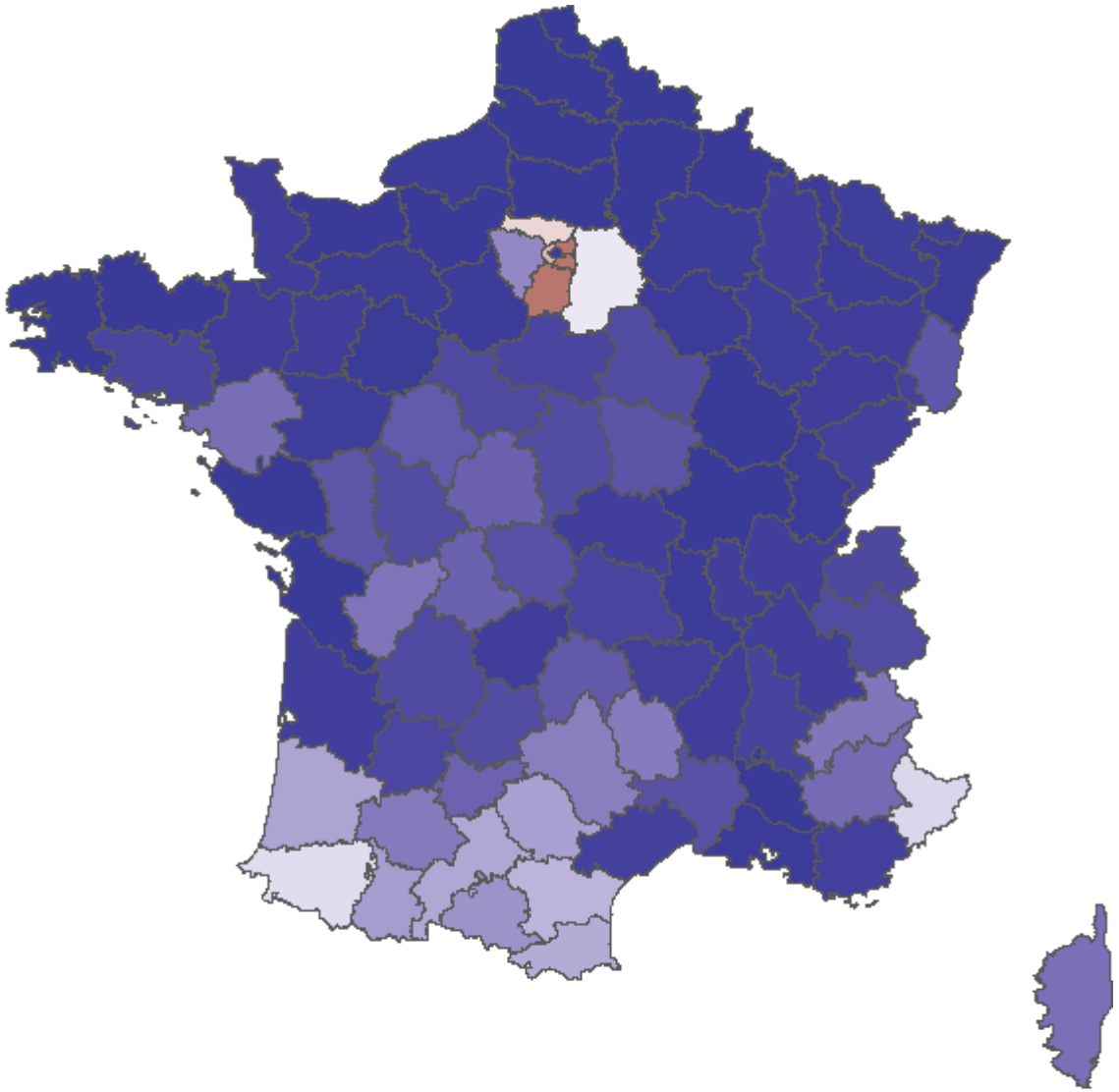
Posterior LB ETI95% expected proportion of GUDs due to HSV-2, assuming the analytical sample had been collected only in each district.

5% 10%



Posterior UB ETI95% expected proportion of GUDs due to HSV-2, assuming the analytical sample had been collected only in each district.

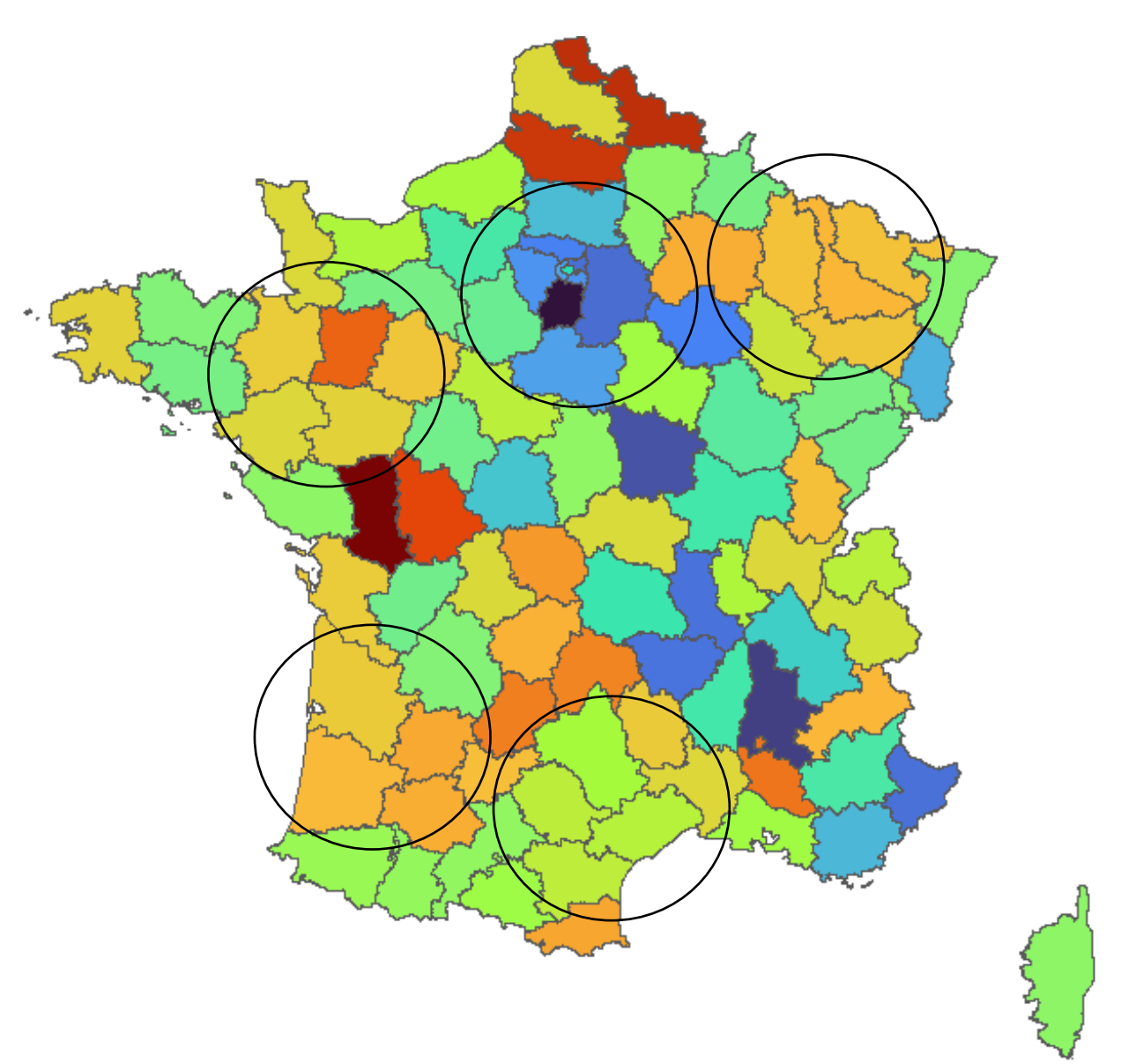
20% 30% 40% 50% 60%



Posterior probability of positive difference in expected proportion of GUDs due to HSV−2, if the analytical sample had been collected only in each district compared with only collected in Paris.

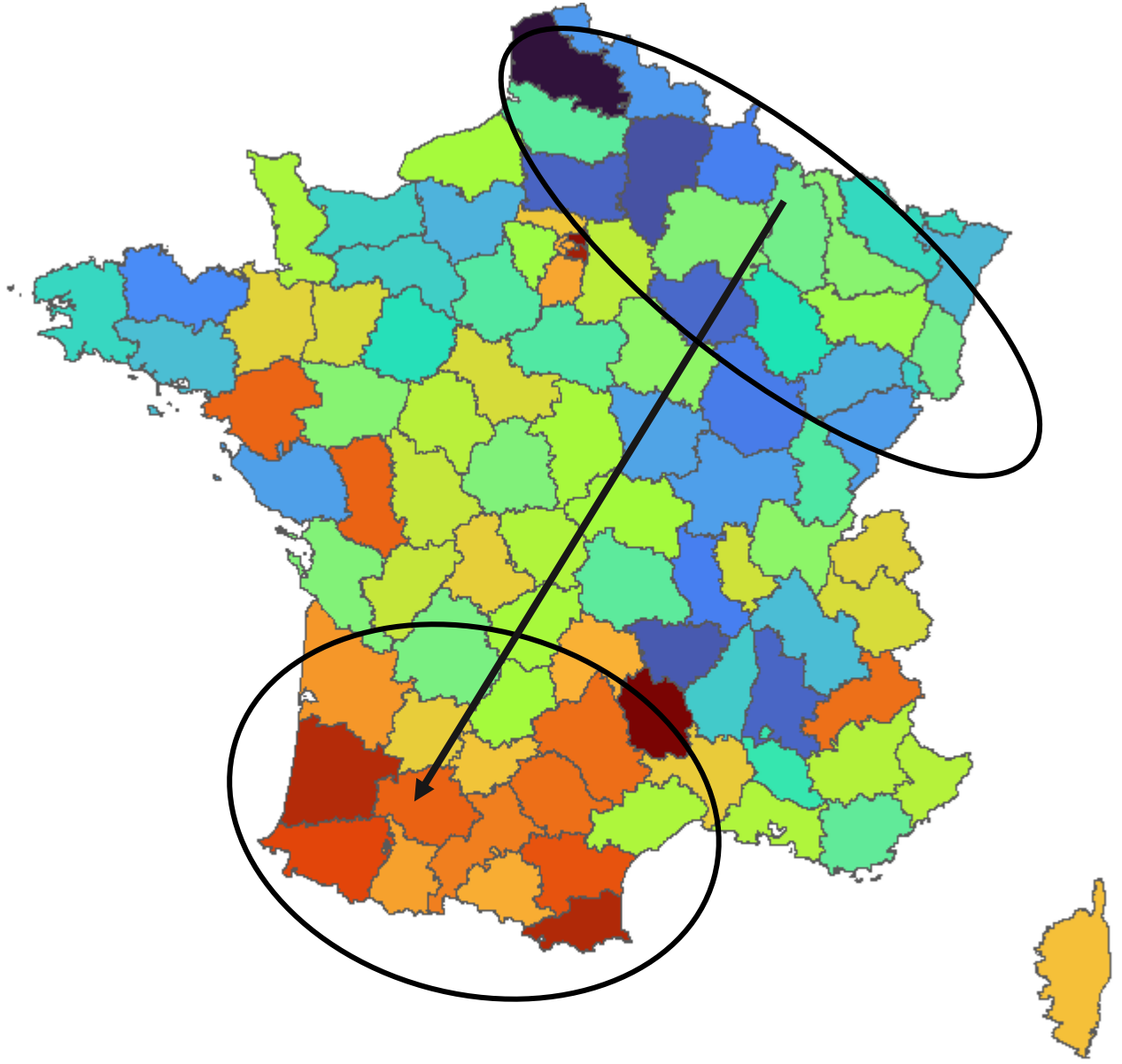
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

Probability threshold	Number of districts with probability > threshold
0.5	74
0.8	26
0.9	0



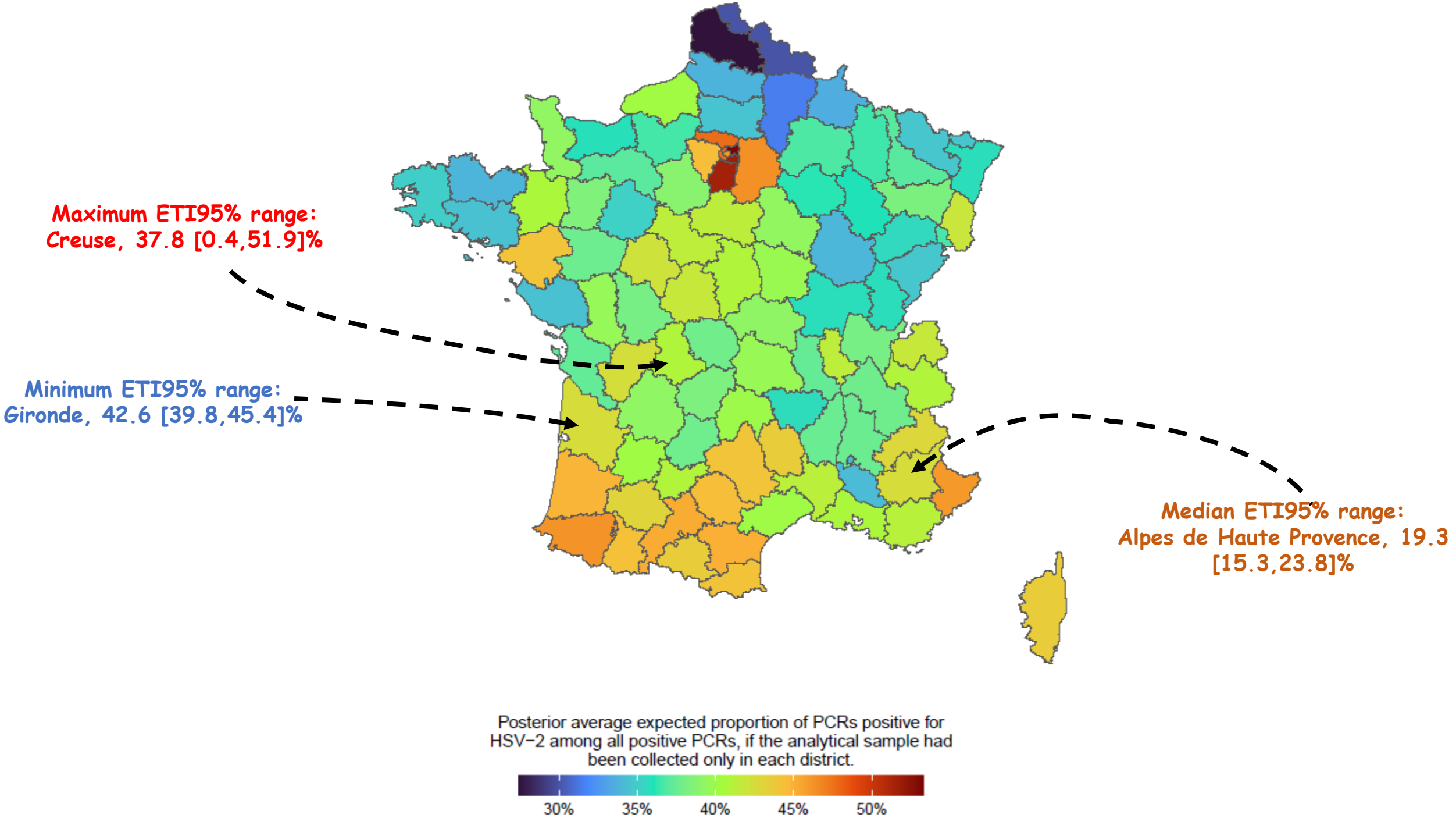
Posterior average expected proportion of GUDs due to HSV−1, assuming the analytical sample had been collected only in each district.

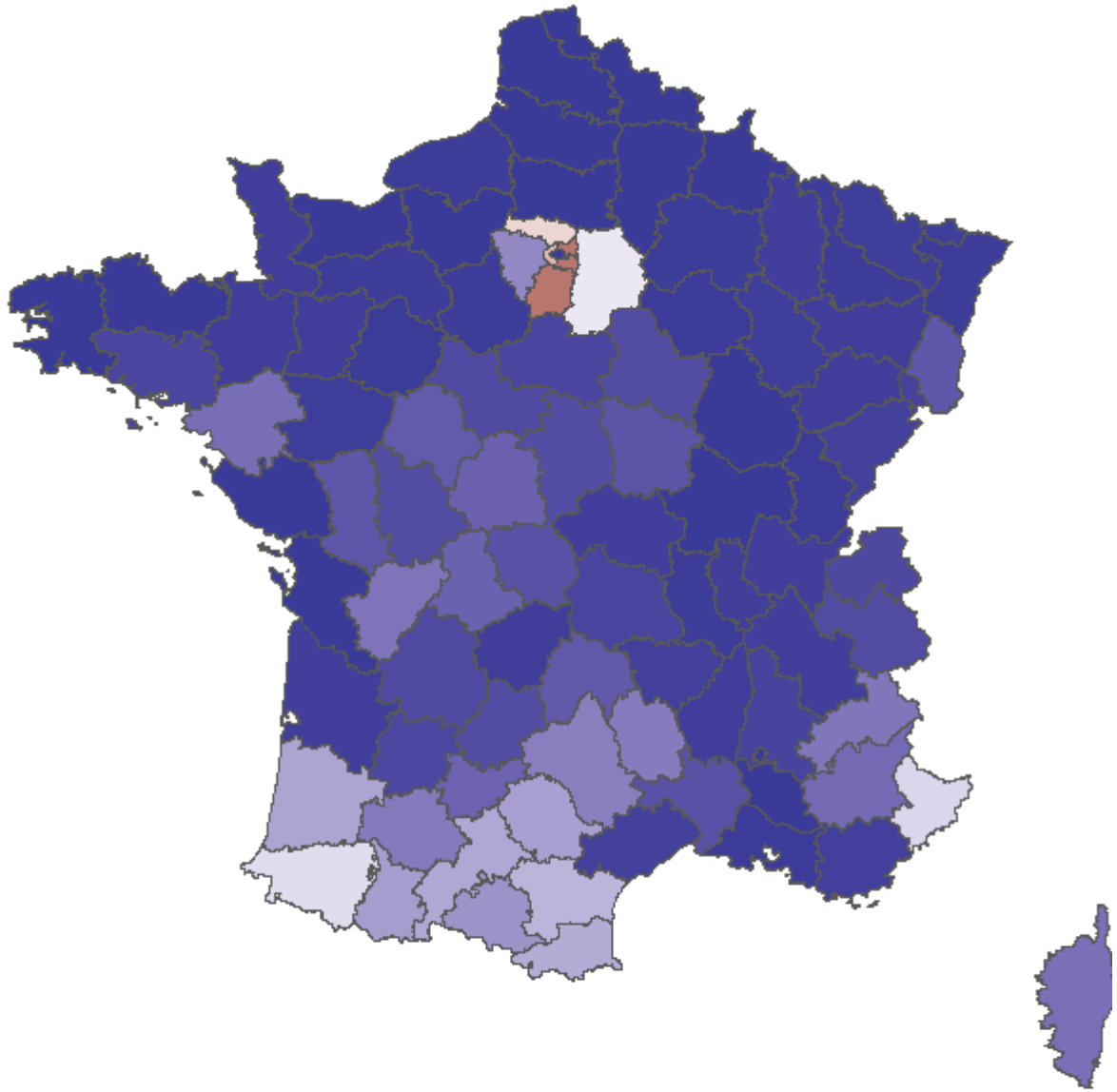
15% 17.5% 20% 22.5% 25%



Posterior average expected proportion of GUDs due to HSV−2, assuming the analytical sample had been collected only in each district.

10% 12% 14% 16% 18%


Maximum ETI95% range:
Creuse, 37.8 [0.4,51.9]%
Minimum ETI95% range:
Gironde, 42.6 [39.8,45.4]%
Median ETI95% range:
Alpes de Haute Provence, 19.3
[15.3,23.8]%
Posterior average expected proportion of PCRs positive for
HSV−2 among all positive PCRs, if the analytical sample had
been collected only in each district.
30%
35%
40%
45%
50%



Probability threshold	Number of districts with probability > threshold
0.5	85
0.8	34
0.9	0

DISCUSSION

				%		
	Country	**Setting**	**N GUDs**	**HSV-1**	**HSV-2**	**HSV-2/(HSV-1+HSV-2)**
This study	FR	Biological laboratories	34,740	18.9 [18.5,19.3]	14.0 [13.7,14.4]	42.6 [41.8,43.4]
Janier et al.	FR	STI clinic in Paris	464	7.8	45.7	
Grange et al.	FR	STI centre (6 different centres)	315	22.9	19.70	
Hope-Rapp et al.	FR	STI clinic in Paris	278	9.4	15.8	
Alareeki et al.	Europe	Meta-analysis	4,173/-/23,323		22.0 [15.3,29.6]	66.0 [62.9,69.1]
Yousuf et al.	Europe	Meta-analysis	800	13.6 [4.1,27.1]		(pour HSV-1: 34.1 [31.7-36.5])

KEY MESSAGE

- Different spatial pattern in the proportion of GUDs due to HSV-1 vs proportion of GUDs due to HSV-2 and the proportion of genital herpes due to HSV-2 (patchiness vs gradient)
- Past studies sampled in areas and setting prone to yield an inflation in the proportion of GUDs/genital herpes due to HSV-2
- Probably this also happened in other countries
- Current pooled estimated are likely upward biased due to poor sampling design

R-SHINY

ongoing work by Ina Câmpan

(intern 1st year Ensae)

Select reference:

Total number of PCR tests (GUDs)

Select virus:

HSV-1

Age:

0 77 100

0 10 20 30 40 50 60 70 80 90 100

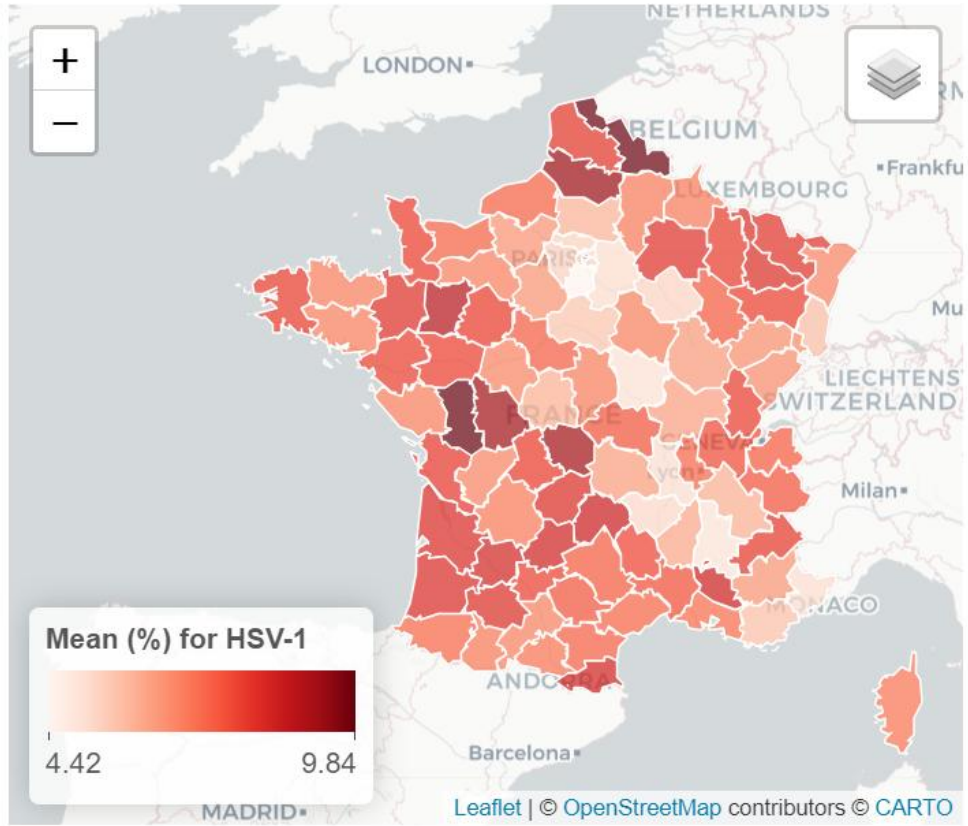
Select variable of interest:

mean

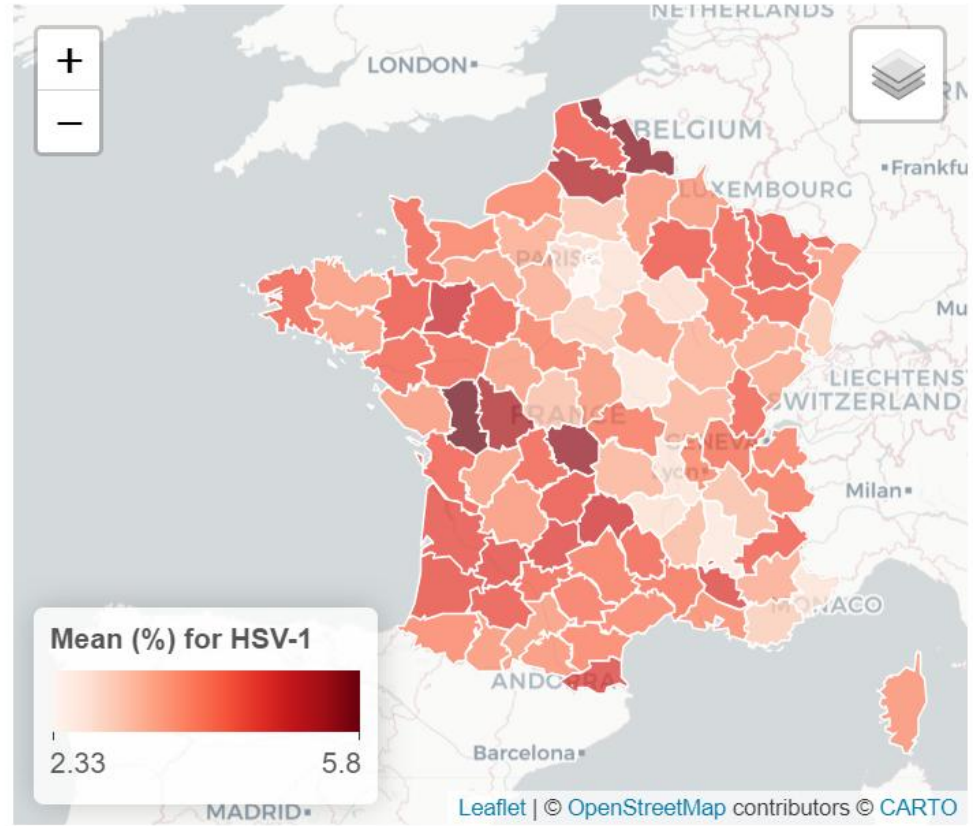
Select week:

Last week of December 2024

Females



Males



Download as HTML

Select reference:

Total number of PCR tests (GUDs)

Select virus:

HSV-1

Select week:

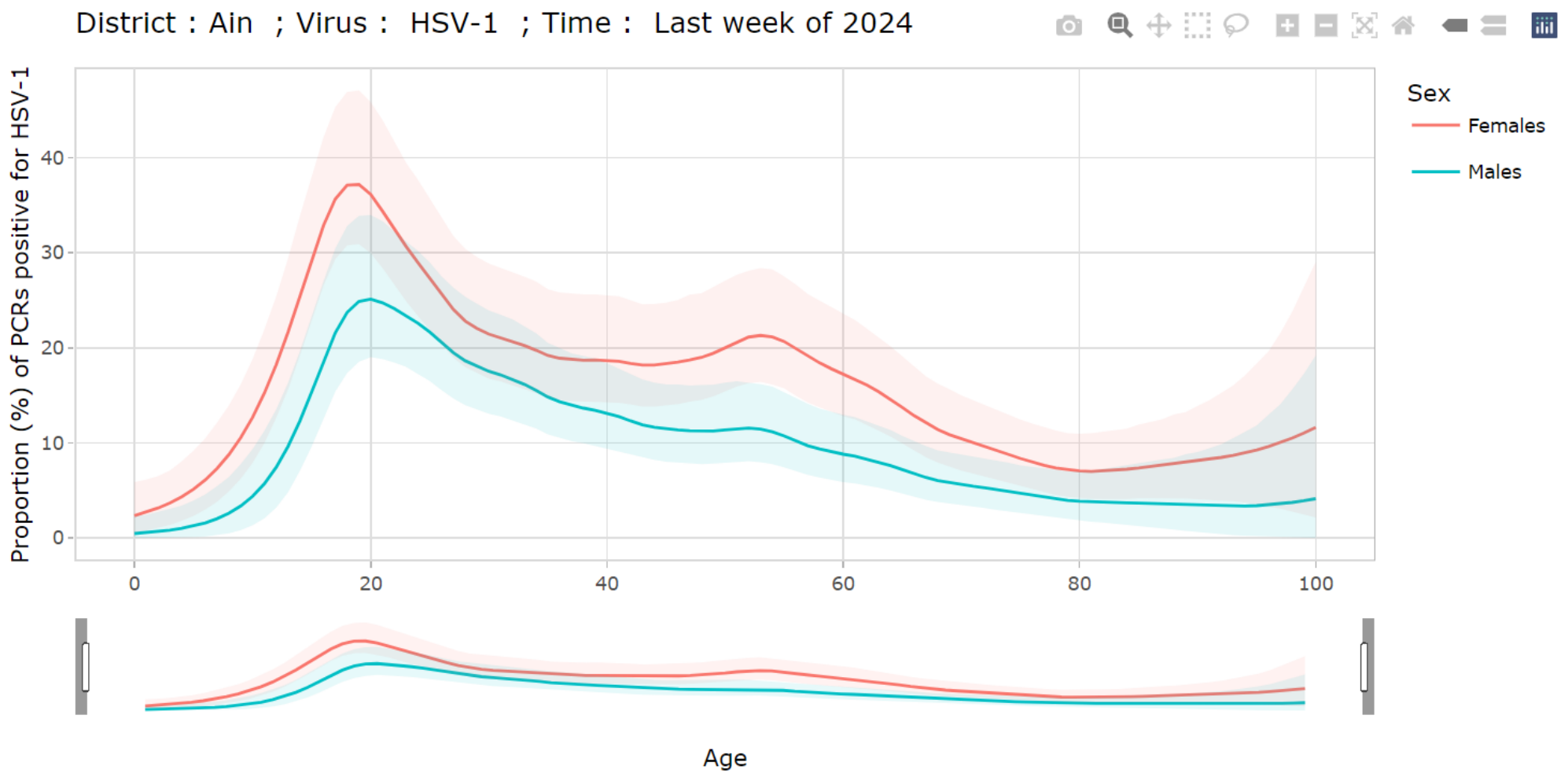
Last week of December 2024

Select district of interest:

Ain

Select weight:

15



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Merci pour votre temps

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- **Research project MIST: ANRS-0681-MIST**

If you have any interest in **prior-data conflict** and have any thoughts you would like to share, please contact me at osupplis@gmail.com