ERN ITHACA

Webinar 2025

European Commission

EUROPEAN REFERENCE NETWORKS

Helping patients with rare or low-prevalence complex diseases

Genetics and Unique Populations: the case of the Finnish, Roma & Irish Travellers

Tuesday14 oct 2025 - 17h00 - 18h30 CEST

Chair by Pr Sally Ann Lynch,

CHI Crumlin & Temple Street, Dublin, Ireland

European Reference Networks ITHACA

Welcome – Technical points

- We are please to be over 121 registrations
- Webinar being recorded

- Thank you for
  - ✓ In case - Turn off your microphone and disconnect your camera
  - ✓ Raise your hand at the time of the questions and discussions
  - ✓ We will answer the questions sent in the registration form
  - ✓ A satisfaction survey at the end of the meeting will be share with you

- Webinars # Recording and PdF will be available on ITHACA's Website
  https://ern-ithaca.eu/documentation/educational-resources/

https://teams.microsoft.com/dl/launcher/launcher.html?url=%2F_%23%2Fl%2Fmeetup-join%2F19%3Ameeting_ZmM1MzY1NTQtMjc4Ni00NmQ4LThmZGEtZjhiMWUyOTc4M2Iz%40thread.v2%2F0%3Fcontext%3D%257b%2522Tid%2522%253a%25222461c129-d44f-406d-a778-d1a3c4c1527c%2522%252c%2522Oid%2522%253a%25223fe3bbab-4860-4b0b-bdc7-6ebc8a2f8f7b%2522%252c%2522prid%2522%253a%25228cb42b1b-7b09-4f60-81d4-3a6e2f877c43%2522%252c%2522isPublic%2522%253atrue%257d%26anon%3Dtrue&type=meetup-join&deeplinkId=21837b08-b4d8-403e-bcbd-9cb3f8e12156&directDl=true&msLaunch=true&enableMobilePage=true&suppressPrompt=true

WG T&E

Anne Hugon Project Manager ERN ITHACA - anne.hugon@aphp.fr

European Reference Networks ITHACA

Webinar introduction

- Genetics and Unique Populations: the case of the Finnish, Roma & Irish Travellers
  - *Europe is made up of many different populations both indigenous to Europe and those that migrated in over the centuries. Differing barriers in healthcare access means that rare and ultra rare disorders may cluster within some of these populations. Some have unique cultural norms that may differ from the general population or may face more difficulty in finding their way to healthcare professionals. It is important for clinicians working with these populations to develop an understanding of the unique issues faced by populations within their locality. How do we reach these communities, and how can the EU help reduce access barriers? This webinar answers these questions by exploring the EU context and the unique needs of these populations.*
  - *Chaired by Pr Sally Ann Lynch.*
- Genetics & Access in Unique Populations
  - Focus: Finnish, Roma, Irish Travellers
  - Rare diseases may cluster in underserved groups due to cultural and healthcare access barriers. How can clinicians and the EU improve outreach and equity?

Agenda

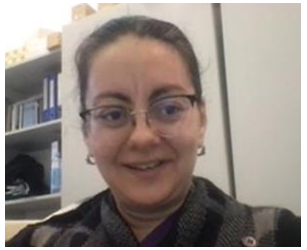
- Welcome and Introduction
  - Sally Ann Lynch, CHI Crumlin & Temple Street, Dublin, Rep of Ireland
- Topic 1- Social determinants of health in European policy
  - Tomas de Jong, European Public Health Alliance (EPHA), Belgium
- Topic 2 - The Finnish story : Founder effects & genetic isolation
  - Outi Kuismin, Oulu University Hospital, Dept of Clinical Genetics and Rare Diseases Unit, Oulu Finland.
- Topic 3 -The Romanian Roma
  - Ioana Streata, Hospital Center, Craiova Romania.
- Topic 4 - The Irish Travellers
  - Sally Ann Lynch, CHI Crumlin & Temple Street, Dublin, Rep of Ireland]
- Time for questions and discussion
  - Conclusion with speakers and moderator

Welcome speakers

- *Sally ann lynch is a clinical professor in genetics based in children's health ireland in Dublin & is attached to University College Dublin. She is the Irish co-ordinator for ERN ITHACA Her research includes work on Irish Travellers & the Roma population.*

- *Tomas de Jong is a Policy Manager with the European Public Health Alliance, where he focuses on their advocacy around health equity, focusing on the social determinants of health, and racism, discrimination, xenophobia and health.*

- *Outi Kuismin, is a clinical geneticist working at the Department of Clinical Genetics at Oulu University Hospital, where I serve as Associate Chief Physician. I also work as a Medical Coordinator in the Rare Diseases Unit. I represent our hospital in the ERN-ITHACA network.*



- *Ioana Streata is an Associate Professor of Cell and Molecular Biology at University of Medicine and Pharmacy from Craiova, Romania, and her research is focused on molecular mechanisms involved in rare developmental disorders. She is also a medical geneticist at the Regional Centre of Medical Genetics Dolj with main activities and responsibilities related to the evaluation, diagnosis, treatment and genetic counselling in genetic disorders.*

Topic 1- Social determinants of health in European policy

Tomas de Jong, European Public Health Alliance (EPHA), Belgium

Social determinants of health in EU policy

European Public Health Alliance
Tomas de Jong
Policy Manager

Who are we?

european public health alliance

European Public Health Alliance (EPHA)

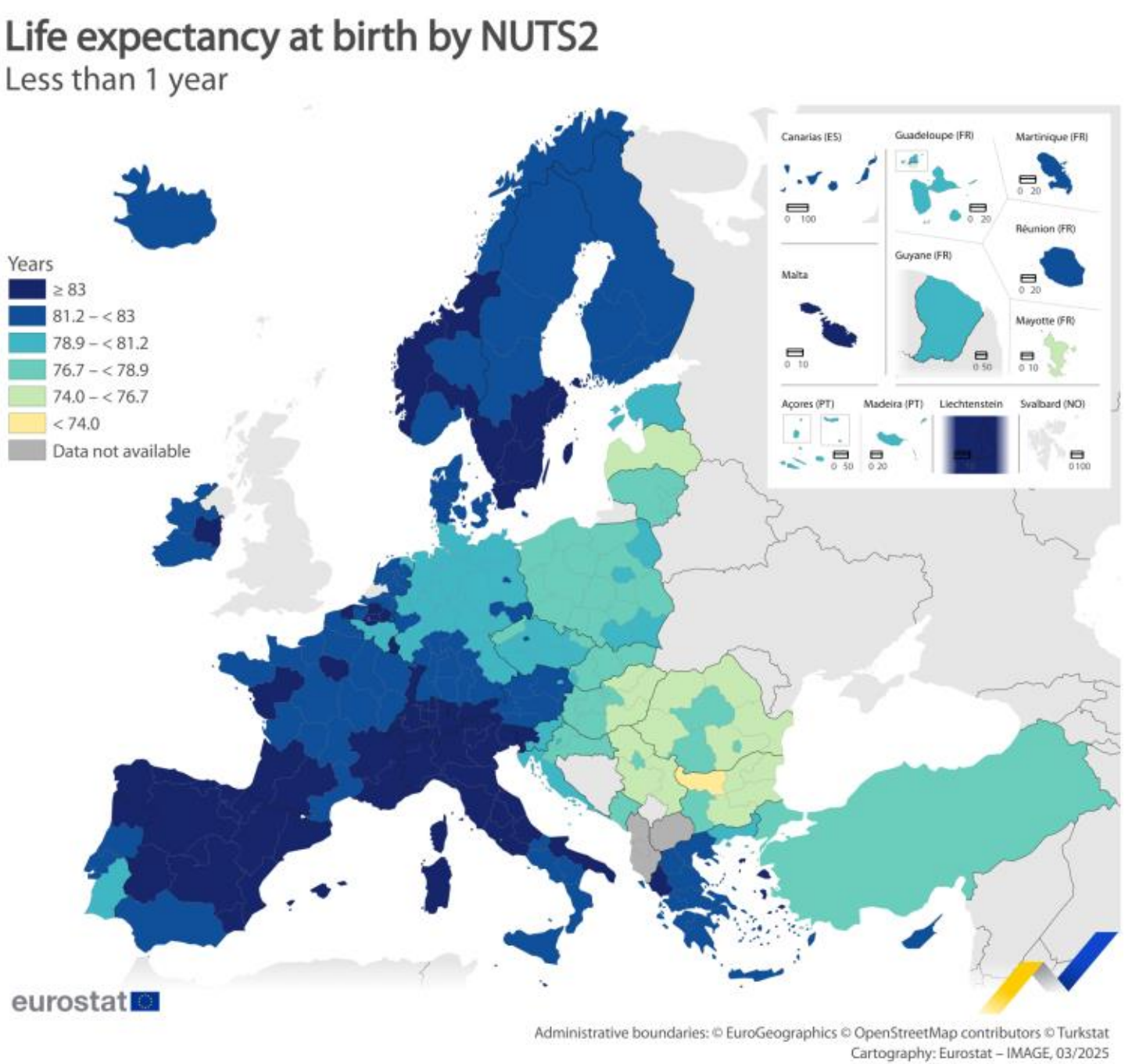
- A change agent for better public health for all in Europe
- Brussels-based membership organisation advocating in the EU policy space
- 40+ members in 20+ countries in WHO European Region
- Members include:
  - Public health civil society
  - Patient organisations and disease groups
  - Health professionals
- Addressing the **determinants of health**

Social determinants

- Social determinants: **non-medical conditions that profoundly impact our ability to be healthy**
  - Our level of education
  - The house we live in
  - Our job
  - Gender, age, race, ethnicity and/or disability status
- Individual effects, but can also **intersect**
- A broad concept – so what does this look like in Europe?

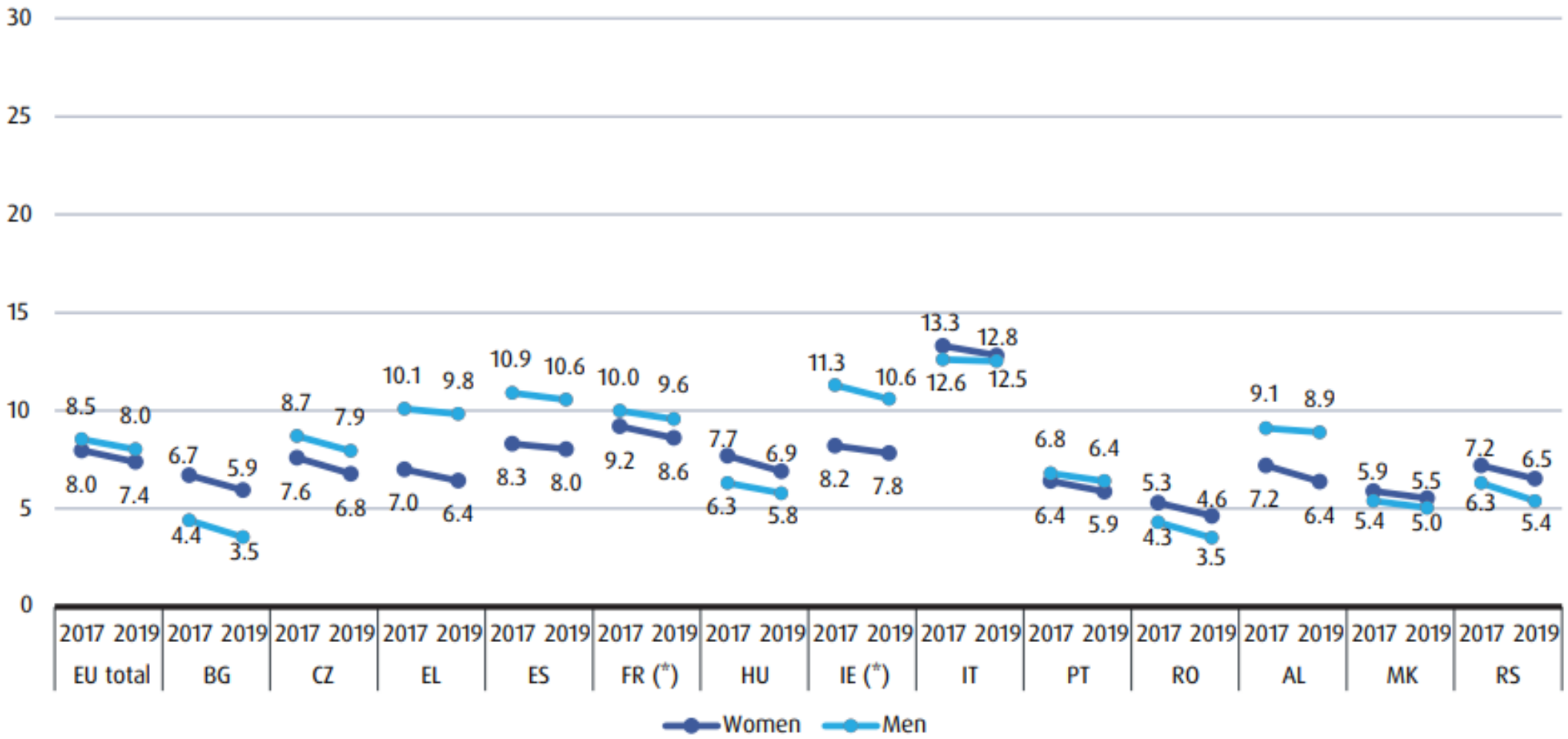
Health Equity

- A case study; **life expectancy**
- Eurostat: a life expectancy gap of **nearly a decade**
  - **86 years** in Comunidad de Madrid, Spain
  - **74 years** in Severozapaden, Bulgaria
- What about **within countries? Populations?**
  - FRA: life expectancy gap faced by Roma and Travellers
    - Roma and Traveller Women: 7.4 years lower
    - Roma and Traveller Men: 8.0 years lower
- The status quo in Europe in 2025?
  - EuroHealthNet and CHAIN: Gap between countries closing, but **“worrying social inequalities in health within countries; inequalities persisted or widened”**



Source: Eurostat, 2025
Mortality and life expectancy statistics

FIGURE 22: GAPS BETWEEN ROMA/TRAVELLERS AND THE GENERAL POPULATION WITH REGARD TO LIFE EXPECTANCY AT BIRTH IN 2017 AND 2019, BY COUNTRY (IN YEARS)



Source: FRA, 2025

Rights of Roma and Travellers in 13 European Countries

Health Equity

- Three case studies of today:
  - **Finland** (Outi Kuismin)
  - **Roma in Romania** (Ioana Streata)
  - **Irish Travellers** (Sally Ann Lynch)
- Some expected issues related to diagnosis and screening:
  - Ability to **reach a clinic**
  - **Trust** in healthcare services
  - **Representation** in research and data
  - **Funding** reaching vulnerable or marginalised communities

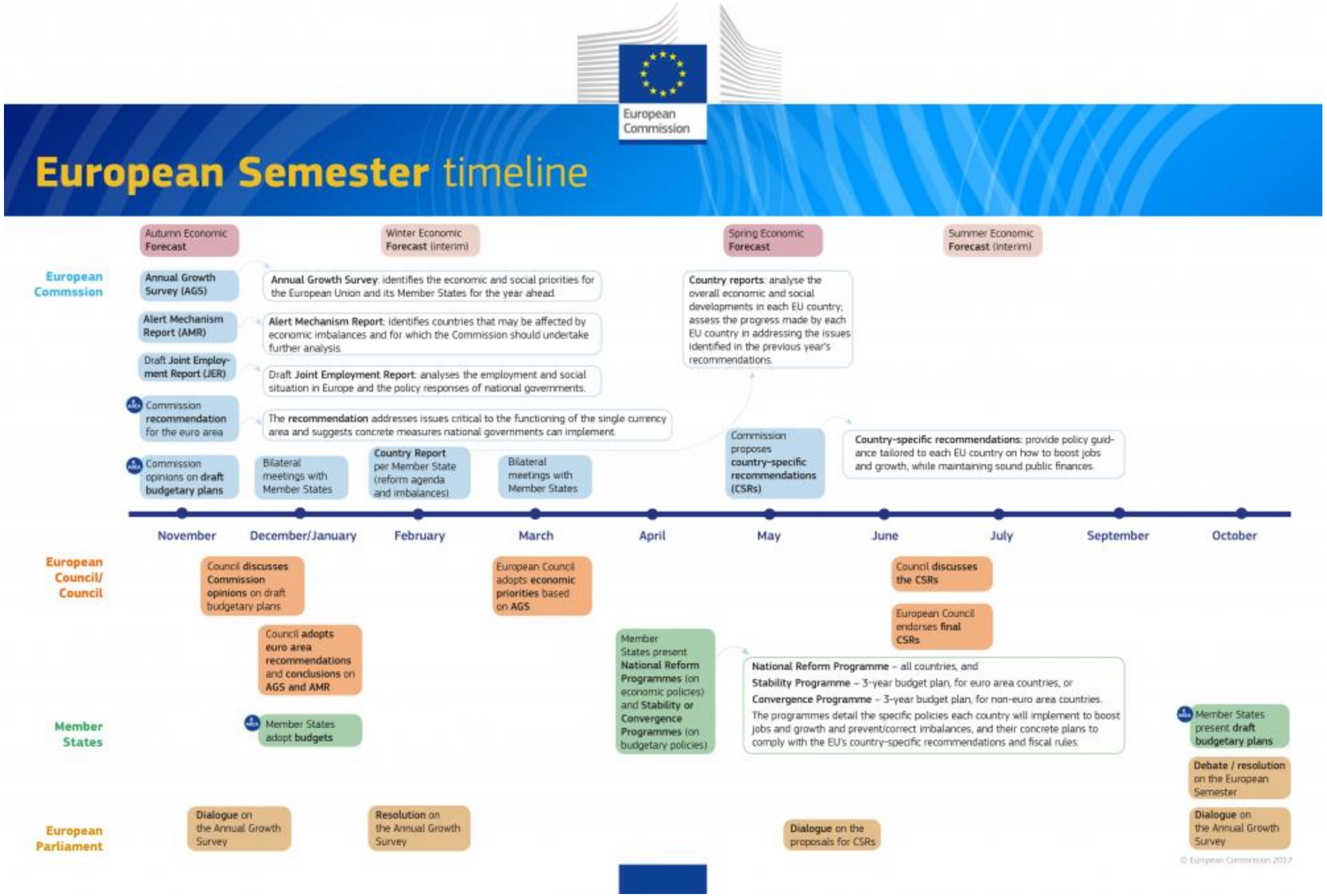
European Policy and Health Equity

- Article 168 TFEU: ““Union action shall respect the **responsibilities of the Member States** for the definition of their health policy and for the organisation and delivery of health services and medical care.”
- That is: health policy is a *national compentence*
- The EU can:
  - Coordinate
  - Guide
  - Reform
- We will focus on
  - **Monitoring and reform**
  - **Inclusion policy**
  - **Data and privacy**

European Policy and Health Equity

Monitoring and reform

- **European Semester**
  - Through the **European Semester:** Europe's *"annual exercise that coordinates the EU's economic and social policies"*
  - A timeline or **roadmap**
- **European Pillar of Social Rights**
  - Action Plan: 20 Principles
  - Principle 16 on Healthcare: "*Everyone has the right to timely access to affordable, preventive and curative healthcare of good quality*"
  - A **compass**


European Commission
European Semester timeline
Autumn Economic Forecast
Winter Economic Forecast (interim)
Spring Economic Forecast
Summer Economic Forecast (interim)
European Commssion
Annual Growth Survey (AGS)
Annual Growth Survey: identifies the economic and social priorities for the European Union and its Member States for the year ahead.
Country reports: analyse the overall economic and social developments in each EU country; assess the progress made by each EU country in addressing the issues identified in the previous year's recommendations.
Alert Mechanism Report (AMR)
Alert Mechanism Report: identifies countries that may be affected by economic imbalances and for which the Commission should undertake further analysis.
Draft Joint Employment Report (JER)
Draft Joint Employment Report: analyses the employment and social situation in Europe and the policy responses of national governments.
Commission recommendation for the euro area
The recommendation addresses issues critical to the functioning of the single currency area and suggests concrete measures national governments can implement.
Commission opinions on draft budgetary plans
Bilateral meetings with Member States
Country Report per Member State (reform agenda and imbalances)
Bilateral meetings with Member States
Commission proposes country-specific recommendations (CSRs)
Country-specific recommendations: provide policy guidance tailored to each EU country on how to boost jobs and growth, while maintaining sound public finances.
November
December/January
February
March
April
May
June
July
September
October
European Council/ Council
Council discusses Commission opinions on draft budgetary plans
European Council adopts economic priorities based on AGS
Council discusses the CSRs
European Council endorses final CSRs
Council adopts euro area recommendations and conclusions on AGS and AMR
Member States present National Reform Programmes (on economic policies) and Stability or Convergence Programmes (on budgetary policies)
National Reform Programme – all countries, and
Stability Programme – 3-year budget plan, for euro area countries, or
Convergence Programme – 3-year budget plan, for non-euro area countries.
The programmes detail the specific policies each country will implement to boost jobs and growth and prevent/correct imbalances, and their concrete plans to comply with the EU's country-specific recommendations and fiscal rules.
Member States
Member States adopt budgets
Member States present draft budgetary plans
Debate / resolution on the European Semester
Dialogue on the Annual Growth Survey
Resolution on the Annual Growth Survey
Dialogue on the proposals for CSRs
Dialogue on the Annual Growth Survey
European Parliament
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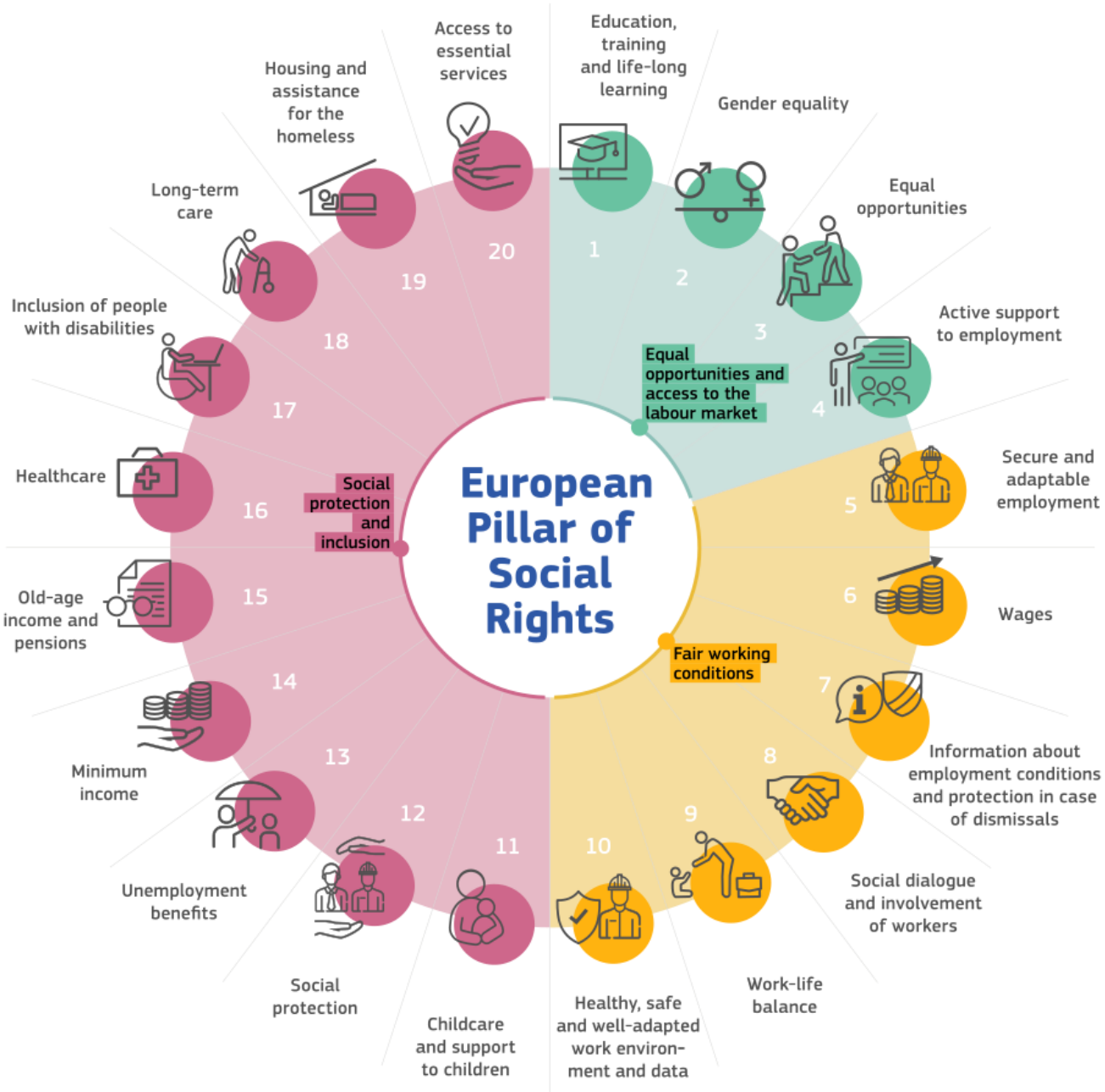
European Pillar of Social Rights
Equal opportunities and access to the labour market
Fair working conditions
Social protection and inclusion
1 Education, training and life-long learning
2 Gender equality
3 Equal opportunities
4 Active support to employment
5 Secure and adaptable employment
6 Wages
7 Information about employment conditions and protection in case of dismissals
8 Social dialogue and involvement of workers
9 Work-life balance
10 Healthy, safe and well-adapted work environment and data
11 Childcare and support to children
12 Social protection
13 Unemployment benefits
14 Minimum income
15 Old-age income and pensions
16 Healthcare
17 Inclusion of people with disabilities
18 Long-term care
19 Housing and assistance for the homeless
20 Access to essential services

European Policy and Health Equity

Inclusion Policy

- Even a perfect healthcare system is ineffective if people are **unable to access it**
- Introduce the **Union of Equality Strategies**
- Example: **EU Roma Strategic Framework**
  - Inclusion of Roma and Travellers at the national level
  - Health goal: "**cut life expectancy gap by at least half**" by 2030
  - E.g. through encouraging **health mediation**
- Other important examples:
  - EU Anti-racism strategy
  - Gender Equality Strategy
  - Strategy for the Rights of Persons with Disabilities

European Policy and Health Equity

Data and privacy

- Inclusion policy → but lack of data **disaggregated by ethnicity**
- Many member states do **not allow collecting ethnicity-based data**
- General Data Protection Regulation **(GDPR)**
  - Relevant for **protecting personal information** and how data is **collected**, **stored** and **used**
- On health data and screening: **European Health Data Space** (EHDS)
  - Focus on **data use** and **collection** for **research** and **policy making**
- Act within both to **inform** inclusive policy and targeted intervention

PERFECTO

- **PERFECTO** – Preventing the Preventable: Familial Hypercholesterolaemia Paediatric Screening for Cardiovascular Health
- EU4Health co-funded project, coordinated by FH Europe
- Focus on FH; a **genetic disorder** that is characterised by **high cholesterol** with increased cardiovascular risk
- Covers:
  - WP2: feasibility of existing and future screening practices
  - WP3: personalised communication model
  - WP4 (EPHA): barriers facing **Roma** in Romania and **migrants** in Cyprus

PERFECTO

- **Inequities** revealed so far:
  - **Access to treatment** across gender and ethnic lines
  - Gaps in **representation** in **research**
  - **Barriers** to genetic testing (cost, awareness, mistrust)
  - **Health literacy** inequities
  - **Gender gaps** in diagnosis and unique risks in treatment

Read more HERE

Conclusion

- **Health equity:** Influenced by **social determinants of health**
- Large inequities **between** and **within countries**
- Broad comprehensive approach through **three angles:**
  1. **Monitoring** and healthcare **reform** (European Semester, EPSR)
  2. **Inclusion** policy (Union of Equality policies and EU Roma Framework)
  3. **Data** and **privacy** (GDPR and European Health Data Space)
- Concrete application example through **PERFECTO**-project
- Keep in mind this **theory of change** during the presentations

*Health inequities are completely **unnecessary** and **avoidable***

Becoming an EPHA member means joining forces to ensure an equitable and healthy future for all.

Find out how:

Contact:
Tomas de Jong
tomas.dejong@epha.org

Stay updated on our latest activities.

Follow our social media channels:

@epha-eu.bsky.social European Public Health Alliance

Thank you!

Topic 2 - The Finnish story : Founder effects & genetic isolation

Outi Kuismin, Oulu University Hospital, Dept of Clinical Genetics and Rare Diseases Unit, Oulu Finland.

The Finnish story : Founder effects & genetic isolation

Outi Kuismin, Oulu University Hospital, Department of Clinical Genetics and Rare Diseases Unit, Finland

ERN-ITHACA WEBINAR: GENETICS AND UNIQUE POPULATIONS: THE CASE OF THE FINNISH, ROMA & IRISH TRAVELLERS

14 October 2025


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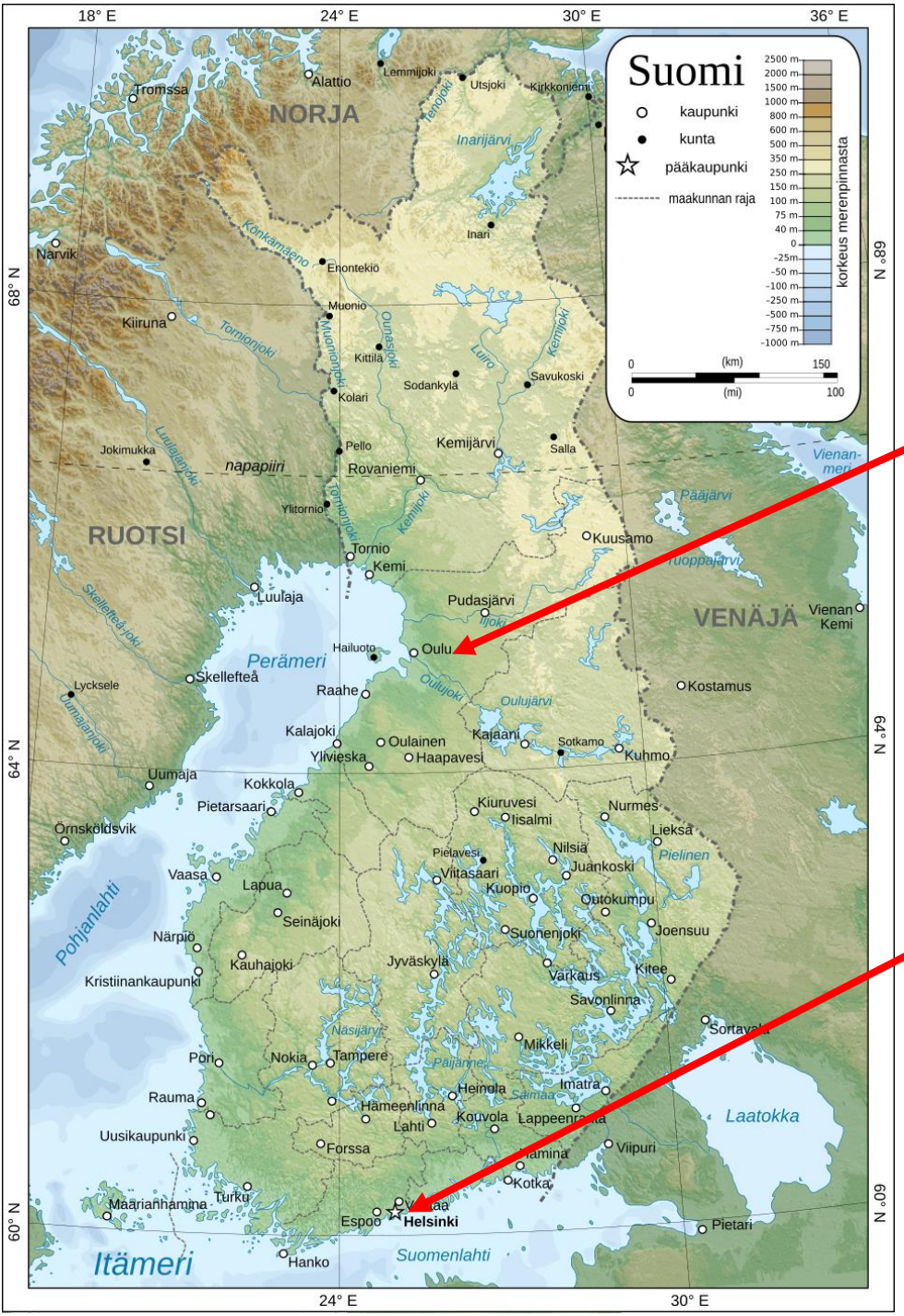


oys Oulu University Hospital

HUS

University hospitals of Oulu and Helsinki are full members of ERN-ITHACA

European Reference Network
for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

ITHACA

Conflict of interests and background

- No commercial interests
- Deputy Chief Physician of Department of Clinical Genetics and Rare Diseases Unit, Oulu University Hospital
- Local coordinator of NFID (Northern Finland Intellectual Disability Cohort) study, PI Professor Aarno Palotie, University of Helsinki
- Research group member of FINNDIG (Genetic Diseases in Northern Finland), PI Professor Jukka Moilanen, University of Oulu
- Representative of Oulu University Hospital in ERN ITHACA and ERN GENTURIS (concortium member)

UNIVERSITY OF OULU

MRC OULU medical research center

oys Oulu University Hospital

Perinnöllisyyslääketieteen klinikka Department of Clinical Genetics

HARVI

The Settlement of Finland

- Finland has been continuously inhabited for about 10,000 years since the last Ice Age.
- Early populations lived by hunting and gathering, numbering in the thousands or tens of thousands. There were no major migration waves—only individual arrivals from the south, east, and west.
- Primitive agriculture began around 4,000 years ago, prompting the Sámi hunter-gatherers to gradually move north. Around 2,000 years ago, more efficient farming led to permanent village settlements and slow population growth.
- Genetically, today's Finns largely descend from this group, which also includes significant ancestry from Yamnaya herders of the Eurasian steppes.

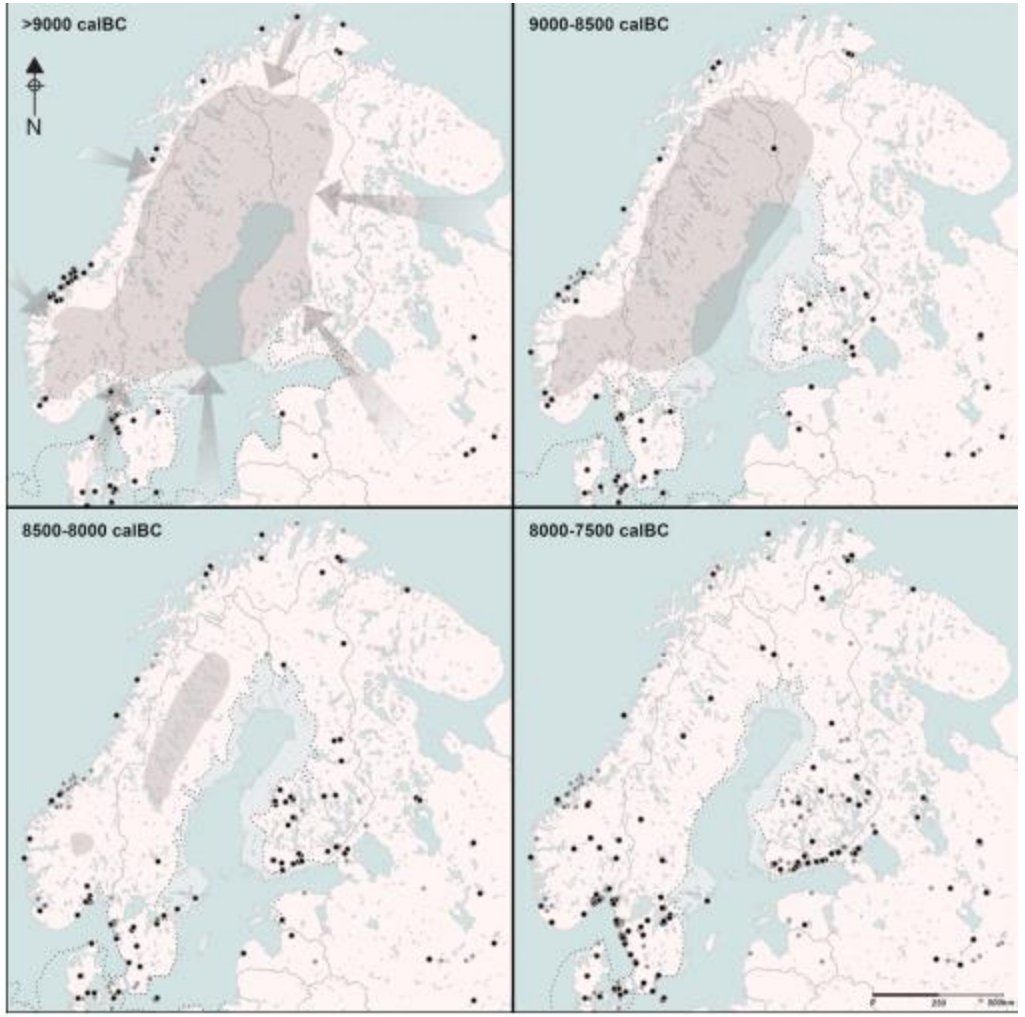


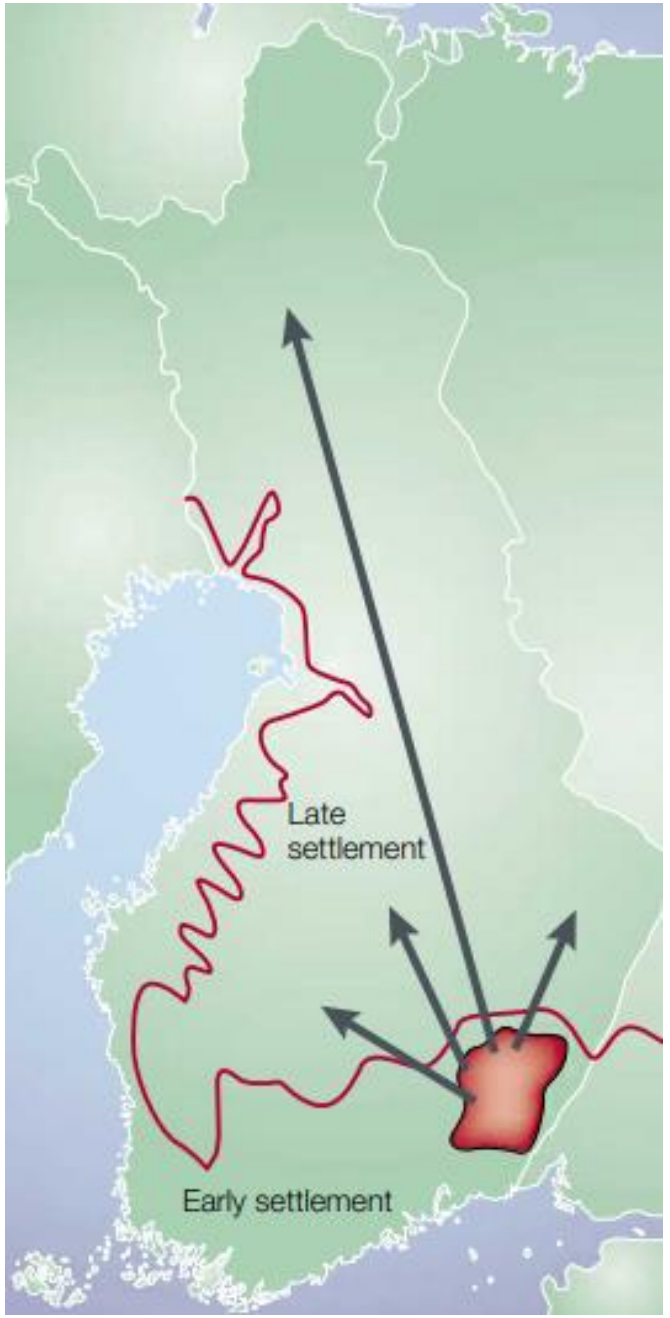
Figure 1. Dated, pre-7500 BC sites (black dots, Table S1) and the retreat of the Scandinavian Ice Sheet (Hughes et al 2016) in four time-slices. Arrows indicate the direction of ice retreat, and grey dots indicate sites from previous time-slice. (maps by M.A. Manninen).

Varilo T. Lääketieteellinen genetiikka. Suomalainen tautiperintö. Duodecim, 2025.

Manninen M.A. et al. First encounters in the north: cultural diversity and gene flow in Early Mesolithic Scandinavia. Antiquity. 2021 Vol. 95 (380): 310–328.

The Settlement of Finland

- A key event in Finland's settlement and disease heritage was the 16th-century south-to-north migration, supported by **Gustav Vasa's rule.**
- The Savonians' slash-and-burn farming led to population growth and forced migration northward.
- This created isolated villages—subisolates—that remained genetically similar until industrialization.
- Marriages were mostly local, roads were absent, and the harsh climate, language barriers, and cultural differences reinforced isolation.
- → FOUNDER EFFECT: a genetic phenomenon where a small group separates from a larger population, leading to reduced genetic diversity. The new group's traits reflect the original few, which can differ significantly from the parent population. This can increase the prevalence of certain inherited diseases.



Peltonen L. et al. Use of population isolates for mapping complex traits. Nat Rev Genet. 2000 Dec;1(3):182-90.

Varilo T. Lääketieteellinen genetiikka. Suomalainen tautiperintö. Duodecim, 2025.

Population bottlenecks

- The crop failures of 1695–97 wiped out nearly half the population

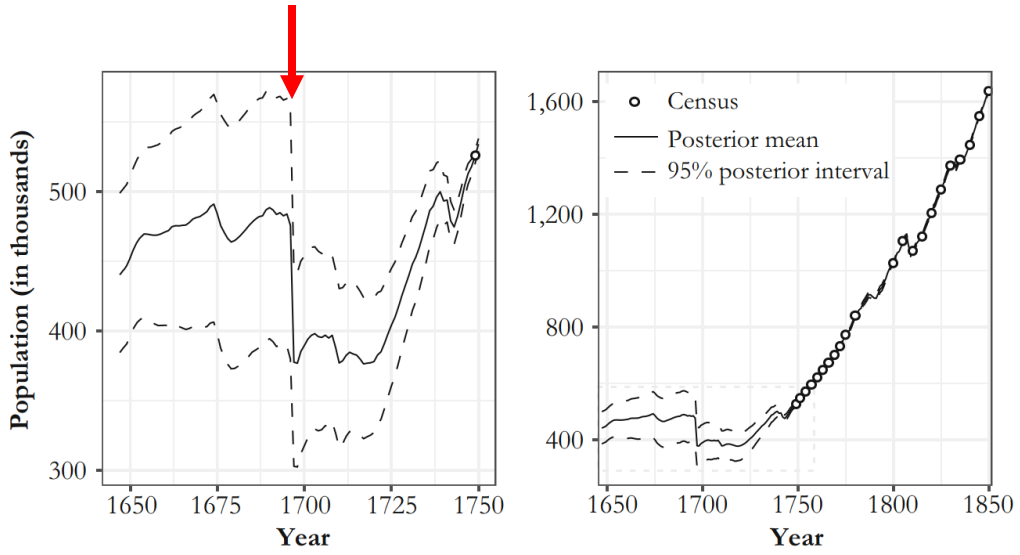
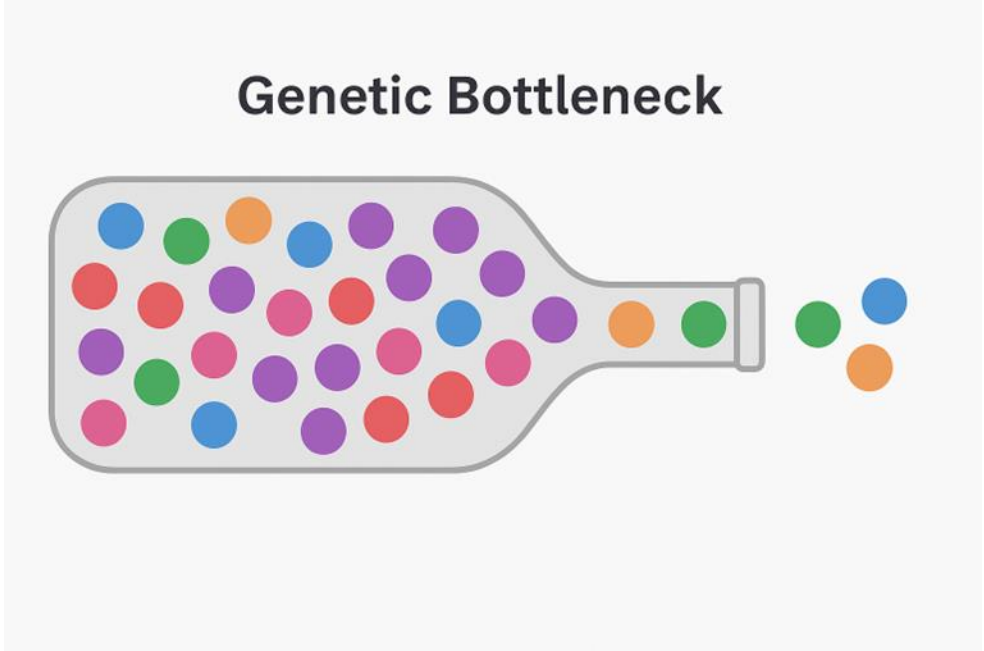


Fig. 5 Estimated Finnish population development (1647–1850). Solid lines represent the posterior means, and dashed lines correspond to the limits of the 95% posterior intervals. Dots mark the census points.

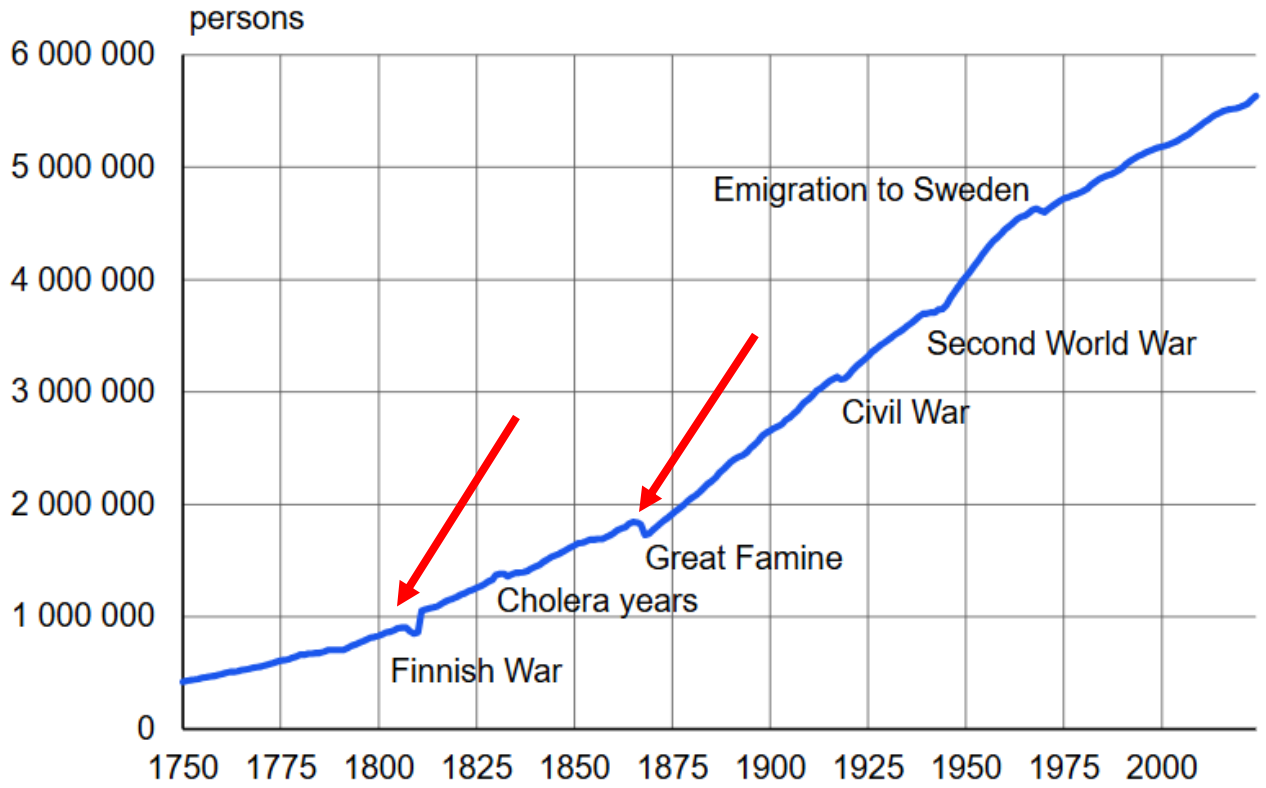
Voutilainen M. et al. A Bayesian Reconstruction of a Historical Population in Finland, 1647–1850



A population bottleneck is an event that drastically reduces the size of a population. It produces a decrease in the gene pool of the population because many alleles, or gene variants, that were present in the original population are lost.

Recent population bottlenecks

Development of population, 1750–2024



Source: Statistics Finland, population structure

- The famine of 1867–68 claimed around 10%, just six generations ago.
- Epidemics and wars also took their toll.
- Rapid population growth began only in the 18th century and accelerated after the 1870s thanks to improved food distribution, infant care, vaccinations, and tuberculosis prevention.

The Finnish Disease Heritage (FDH)

- The FDH refers to a group of inherited disorders caused by single-gene mutations that are unusually common in Finland.
- In many cases, there are more patients in Finland than in the rest of the world combined.
- Random genetic drift and the founder effect have enriched the country with around 40 mainly recessively inherited diseases.
- Only diseases found in at least ten families have been included.
- The combined birth incidence of recessively inherited diseases belonging to the FDH is estimated to be around 0.1%. Without preventive measures, this would mean approximately 50–60 affected children born each year

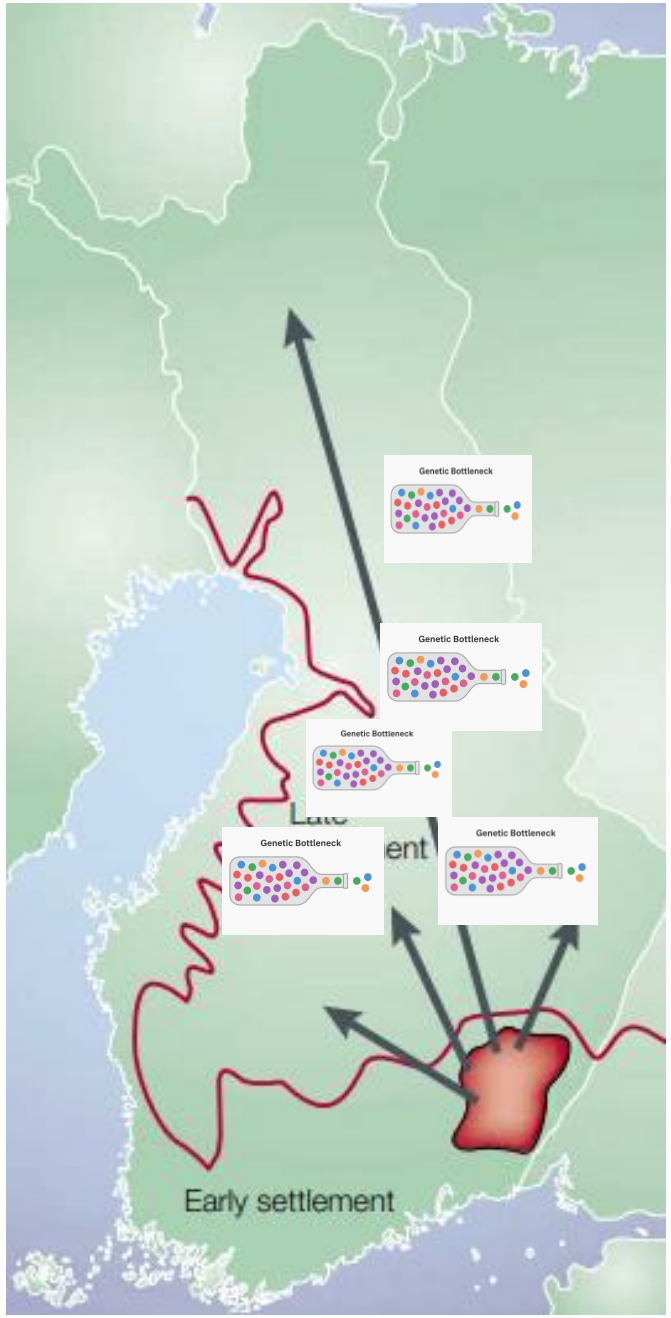
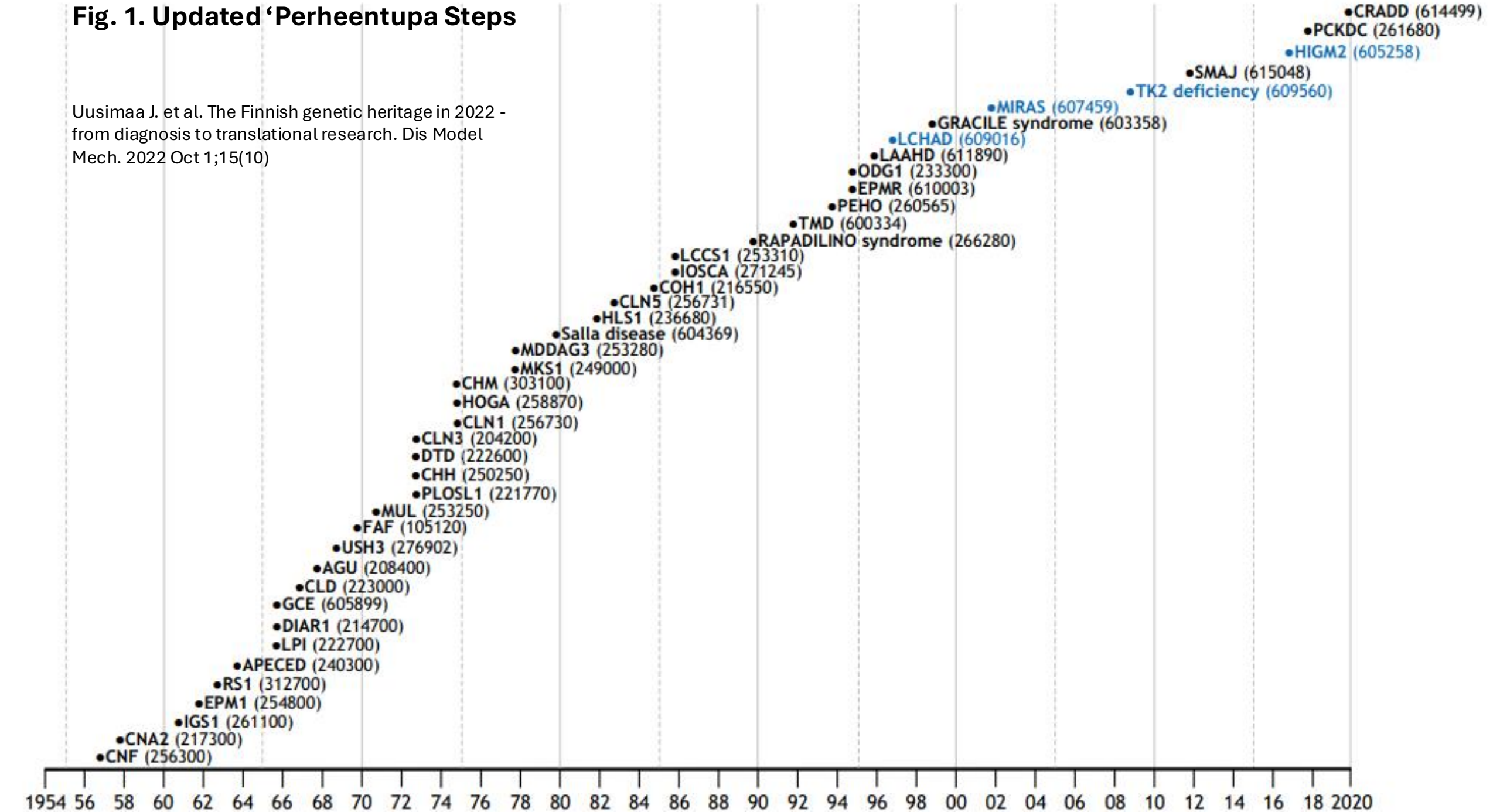


Fig. 1. Updated ‘Perheentupa Steps

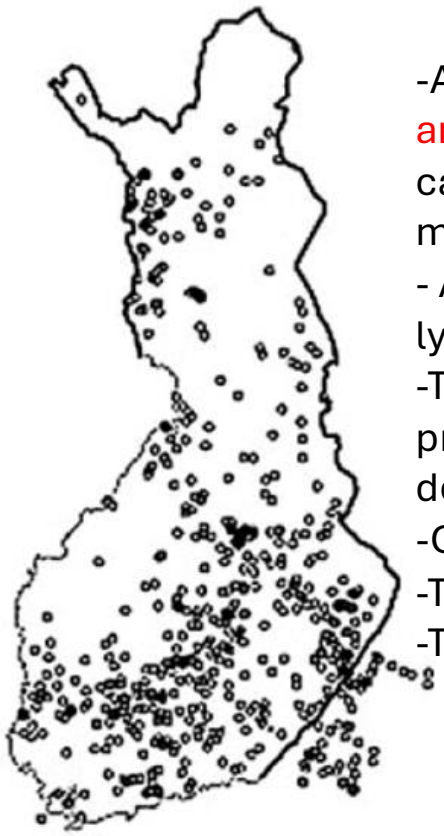
Uusimaa J. et al. The Finnish genetic heritage in 2022 - from diagnosis to translational research. Dis Model Mech. 2022 Oct 1;15(10)



Brain damage disorders	Fatal infant disordes	Eye diseases	Growth disorders	Gastrointestinal/ metabolic disorders	Other diseases
▪ Frontotemporal pachygyria ▪ Aspartylglucosaminuria ▪ Cohen syndrome ▪ Epilepsy, progressive with mental retardation ▪ Epilepsy, progressive myoclonic, 1 ▪ Ceroid lipofuscinosis, neuronal, 1 ▪ Infantile onset spinocerebellar ataxia ▪ Ceroid lipofuscinosis, neuronal, 3 ▪ Ceroid lipofuscinosis, neuronal, 5 ▪ Muscular dystrophy-dystroglycanopathy type a, 3 ▪ Glycine encephalopathy ▪ Progressive encephalopathy with edema, hypsarrhythmia and optic atrophy ▪ Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy 1 ▪ Salla disease	• GRACILE • Hydrolethalus • Lethal congenital contracture syndrome 1 • Lethal arthrogryposis with anterior horn cell disease • Meckel syndrome type 1 • Finnish congenital nephrosis	▪ Choroideremia ▪ Cornea plana 2 ▪ Hyperornithinemia with gyrate atrophy of choroid and retina ▪ Retinoschisis ▪ Usher syndrome, type III ▪ Amyloidosis, Finnish type	▪ Cartilage-hair hypoplasia ▪ Diastrophic dysplasia ▪ Mulibrey-nanism ▪ RAPADILINO	▪ Diarrhea, secretory chloride, congenital ▪ Lactase deficiency, congenital ▪ Lysinuric protein intolerance ▪ Phosphoenolpyruvate carboxykinase deficiency, cytosolic ▪ Imerslund-Grasbeck syndrome 1	▪ Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy ▪ Ovarian dysgenesis 1 ▪ Bone marrow failure syndrome 2 ▪ Tibial muscular dystrophy ▪ Spinal muscular atrophy, Jokela type (SMAJ)

Mutation class relative to age	When passed through genetic bottleneck	Birthplaces of patients' ancestors	General characteristics
Young	20–30 generations ago. (in the 15th-17thcentury)	Often concentrated in one specific geographical area.	Local carrier frequency can be very different from the average carrier frequency in the Finnish population.
Middle-aged	30–40 generations ago. (in the 13th-15th century)	Follow a fan-shaped pattern from southeast to north, reflecting the migration wave of the 16th century.	These mutations are responsible for most of the diseases.
Old	80–120 generations ago. (~2,000 years ago.)	Reflect the population density. Thought to represent the carrier diversity of the original population around the time when village settlements became established.	These diseases are the most common within the Finnish disease heritage.

Aspartylglucosaminuria, AGU

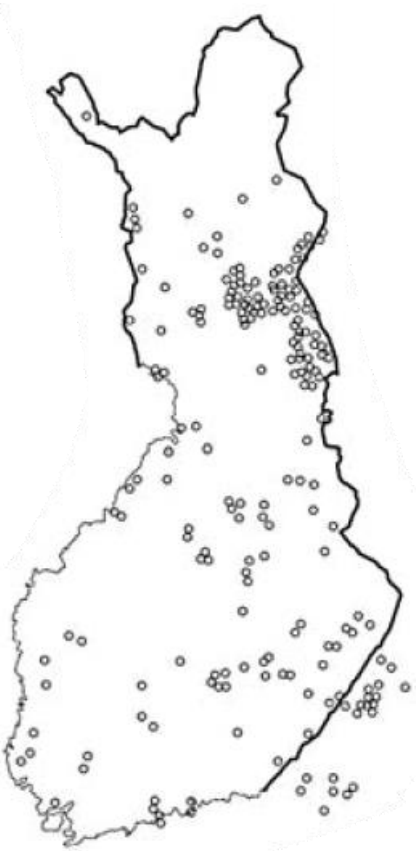


-Amongst the Finnish AGU patients 98% are homozygous for the variant which is called the AGU Fin major (*AGA* c.488G>C,p. Cys163Ser)
- AGU is a severe autosomal recessive lysosomal storage disorder
-The most characteristic feature is progressive impaired intellectual development.
-One of the old mutations
-The carrier frequency is 1/65
-The prevalence is 1/17 000 (in Finland)

Genetic Ancestry Group	Allele Count	Allele Number	Number of Homozygotes	Allele Frequency
South Asian	0	90822	0	0.000
Remaining	27	62130	0	0.0004346
Middle Eastern	0	6046	0	0.000
European (non-Finnish)	37	1169066	0	0.00003165
European (Finnish)	491	63992	0	0.007673
East Asian	0	44832	0	0.000
Ashkenazi Jewish	0	29544	0	0.000
Amish	0	910	0	0.000
African/African Americ	0	74832	0	0.000
Admixed American	0	59992	0	0.000
XX	279	805524	0	0.0003464
XY	276	796642	0	0.0003465
Total	555	1602166	0	0.0003464

The *AGA* c.488G>C,p. Cys163Ser variant is 242 x more prevalent in the Finnish gnomAD cohort compared to non-Finnish Europeans.

Salla disease, Sialuria (Finnish type)



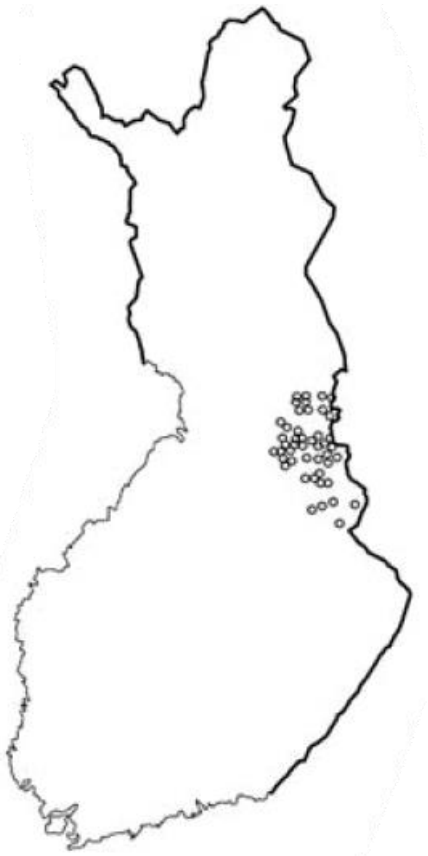
-In the Finnish population, ca. 95% of Salla disease patients are homozygous for the *SLC17A5* c.115C>T, p.(Arg39Cys).
-Salla disease is characterized by slowly progressive neurologic deterioration resulting in mild-to-moderate intellectual disability, spasticity, athetosis, and epileptic seizures.
-One of the middle-aged mutations.
-The carrier frequency is 1/90
-The prevalence is 1/35 000

gnomAD v4.1.0, SNV:6-73644583-G-A(GRCh38)

Genetic Ancestry Group	Allele Count	Allele Number	Number of Homozygotes	Allele Frequency
European (Finnish)	292	64016	1	0.004561
Remaining	21	62496	0	0.0003360
European (non-Finnish)	272	1179922	0	0.0002305
Admixed American	1	60018	0	0.00001666
African/African American	1	75046	0	0.00001333
South Asian	1	91068	0	0.00001098
Ashkenazi Jewish	0	29598	0	0.000
East Asian	0	44870	0	0.000
Middle Eastern	0	6058	0	0.000
Amish	0	912	0	0.000
XX	287	812378	1	0.0003533
XY	301	801626	0	0.0003755
Total	588	1614004	1	0.0003643

The *SLC17A5* c.115C>T, p.(Arg39Cys) variant is 19.8 x more prevalent in the Finnish gnomAD cohort compared to non-Finnish Europeans.

Epilepsy, progressive, with mental retardation (EPMR) = Northern epilepsy



-98 % of the Northern epilepsy patients are homozygotes for the variant *CLN8*, c.70C>G (p.Arg24Gly)
-Epileptic seizures manifest at five to ten years of age, become more frequent at puberty and diminish in adult age. Mental development begins to deteriorate two to five years after manifestation of the seizures and proceeds to mental retardation.
-One of the young mutations
-Carrier frequency; 1/500? Local carrier frequency must be higher in Kainuu region.
-The prevalence is 1/180 000

Genetic Ancestry Group	Allele Count	Allele Number	Number of Homozygotes	Allele Frequency
European (Finnish)	68	63990	0	0.001063
African/African American	0	74836	0	0.000
Admixed American	0	59972	0	0.000
Ashkenazi Jewish	0	29608	0	0.000
East Asian	0	44854	0	0.000
Middle Eastern	0	6082	0	0.000
European (non-Finnish)	0	1180012	0	0.000
Amish	0	912	0	0.000
South Asian	0	91058	0	0.000
Remaining	0	62482	0	0.000
XX	37	812380	0	0.00004555
XY	31	801426	0	0.00003868
Total	68	1613806	0	0.00004214

The *CLN8*, c.70C>G (p.Arg24Gly) variant is found only in the Finnish cohort in gnomAD v4.1.0

In conclusion

Table 1 At-risk couple frequencies for genetic ancestry groups in gnomAD v4.0, calculated for genes with a GCF ≥ 0.5% and all genes

Genetic Ancestry Group	AR Genes With GCF ≥ 0.5%	All AR Genes	All XLR/XL Genes Without *G6PD*, *FGD1*, v4.0 Genomes
AFR	3.48%	3.72%	0.91%
AMR	1.37%	1.67%	0.98%
ASJ	6.11%	6.26%	1.18%
EAS	2.97%	3.20%	2.56%
FIN	2.88%	3.02%	0.54%
MID*	1.79%	1.99%	0.93%
NFE	3.50%	3.78%	1.01%
SAS	1.14%	1.35%	1.90%

G6PD deficiency is a quite mild disorder with very high carrier frequencies. We therefore decided to exclude this gene from the ACF calculations. *G6PD* is not recommended for carrier screening by ACMG.

The sample size of Middle Eastern genetic ancestry group ($N = 147$) is too small to reliably evaluate carrier frequencies. We therefore present v4.0 exome results for this genetic ancestry group.

AFR, African/African American; *AMR*, Admixed American; *ASJ*, Ashkenazi Jewish; *EAS*, East Asian; *FIN*, Finnish; *MID*, Middle Eastern; *NFE*, European (non-Finnish); *SAS*, South Asian.

→Finns do not differ from other ethnic groups in the overall risk of recessively inherited diseases

→The difference lies in the spectrum of diseases.

→Many diseases that are common elsewhere are rare in Finland.

Hotakainen R. et al. Estimation of carrier frequencies of autosomal and X-linked recessive genetic conditions based on gnomAD v4.0 data in different ancestries. Genetics in Medicine (2025) 27, 101304

Thank you for your attention!

outi.kuismin@pohde.fi

Topic 3 -The Romanian Roma Genetic and Scientific Insights

Ioana Streata, Emergency Clinical County Hospital Center, Craiova Romania.

GENETIC STUDY OF UNIQUE POPULATIONS

Helps understanding

- Human migration
- Disease risks
- Population history

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INTRODUCTION

1

The Roma are one of Europe's largest ethnic minorities (~10–12 million people).

2

In Romania: estimates range from **1.5 to 2 million** Roma (officially ~600,000).

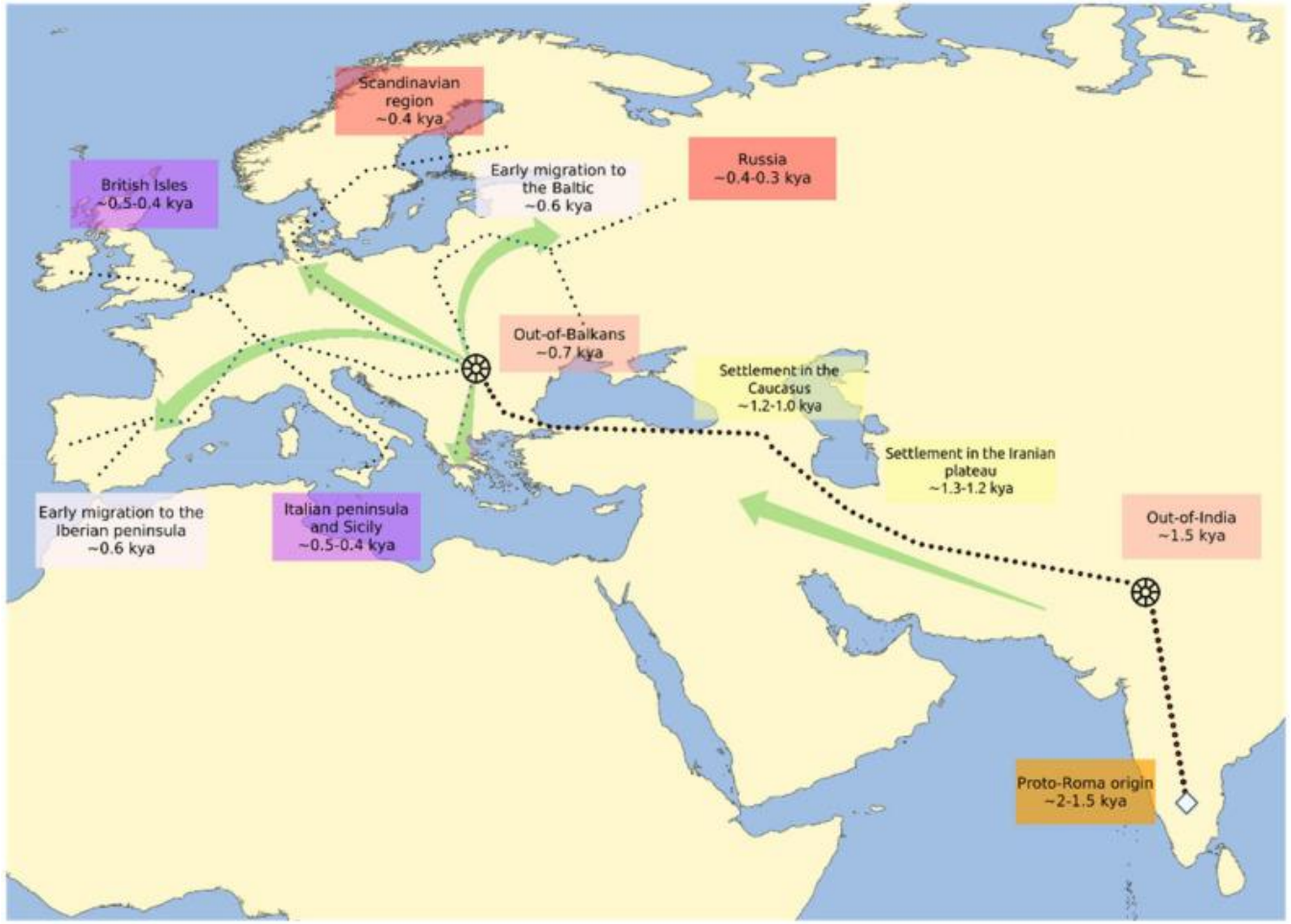
3

Known for rich cultural diversity and complex historical migration routes.

4

Scientifically, the Roma population offers a unique model for **population genetics, admixture, and founder effects**.

ORIGINS AND MIGRATION



Early routes of the Romani diaspora - https://doi.org/10.3390/genes13112068

- **South Asian origin** (~1,000 years ago): genomic evidence links Roma ancestry to northwestern India.
- Migration through **Persia → Armenia → the Balkans → Central and Eastern Europe.**
- Arrival in Romania: ~14th century.
- Genetic drift and bottlenecks occurred along migration routes.

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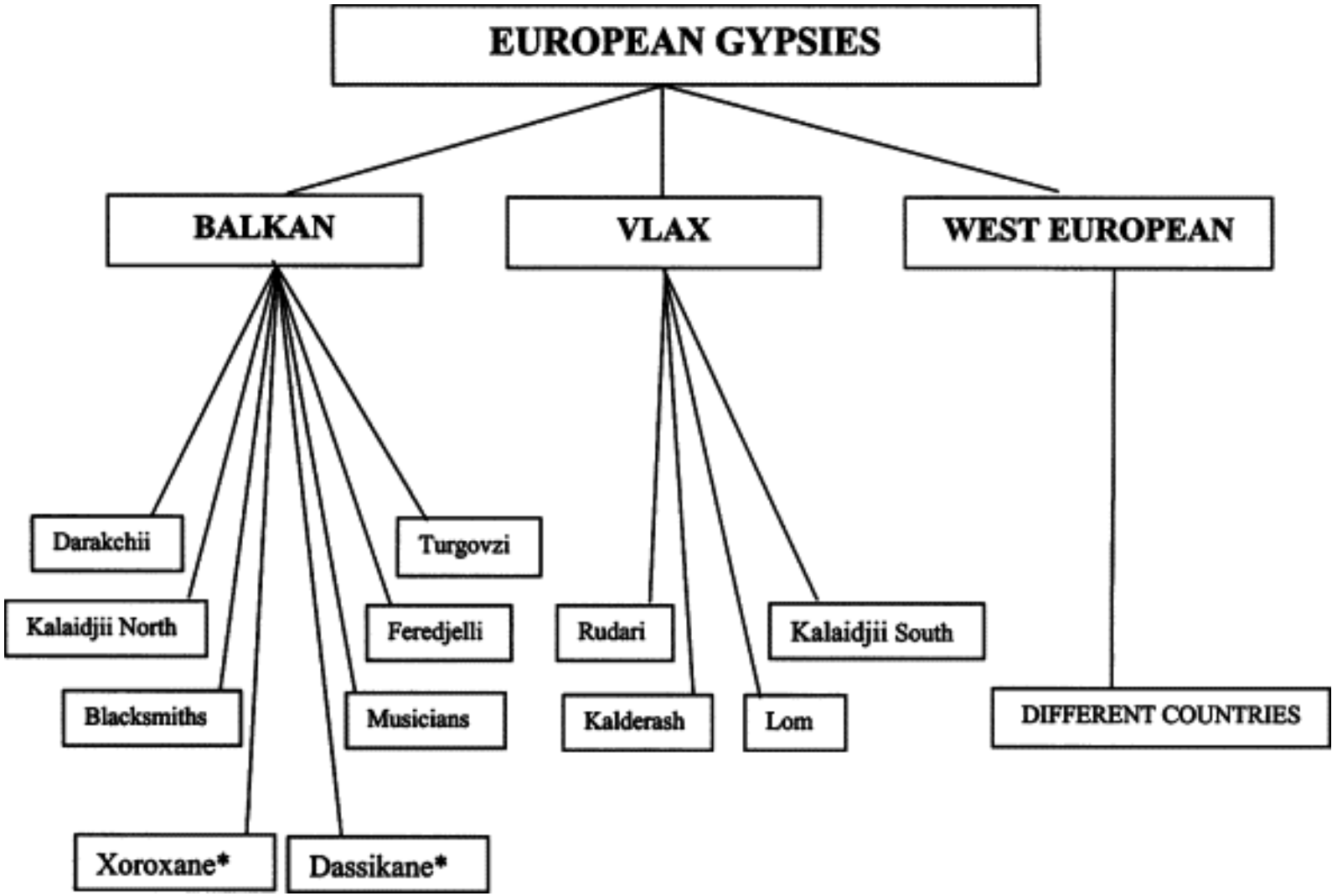
STRUCTURE OF ROMA POPULATIONS



Examples of Roma subgroups

LIFE EXPECTANCY

The Roma population is demographically different from the majority European populations insofar as it is noticeably younger – and consistently so across Europe.

Life expectancy data is very limited on a national and regional level. Most data are based upon estimates. The most widely cited data stems from the Council of Europe.

Roma experience substantially lower (up to 20 years) life expectancy compared to non-Roma.

Some evidence exists suggesting that shorter life expectancy in Roma people

occurs as a result of the broader environmental conditions they experience.

- Higher rates of infant mortality are reported in some Roma populations (those living in poor housing, with low educational levels and migrant Roma) compared to non-Roma

PREVALENCE OF MAJOR INFECTIOUS DISEASE AND IMMUNISATION UPTAKE

A group of Romani people in Bucharest, Romania, 1865

higher rates of infectious diseases or risk of infectious disease outbreaks amongst Roma, particularly segregated Roma, compared to the majority population (including Measles and Hepatitis A).

Evidence relating to rates of HIV/Aids is more mixed, though some findings report faster disease progression.

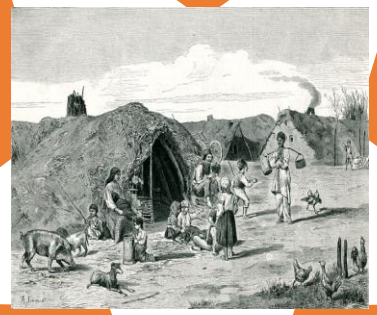
There is a lack of data on vaccination uptake in the Roma population.

The available evidence suggests that with some exceptions (Croatia, Hungary, and the Czech Republic) the Roma population, particularly migrant Roma, have lower or much lower rates of childhood vaccination uptake.

HEALTHY LIFESTYLES AND BEHAVIOURS

Roma suffer disproportionately from illnesses that are associated with the social determinants of health.

negative impact on the health lifestyles of Roma.



Available data on diet and physical activity consistently suggest that healthy diet and physical activities to stay healthy are less common in Roma people.

Small scale studies have identified a number of cultural factors which have a

Available data on smoking prevalence consistently show smoking is more common in the Roma population.

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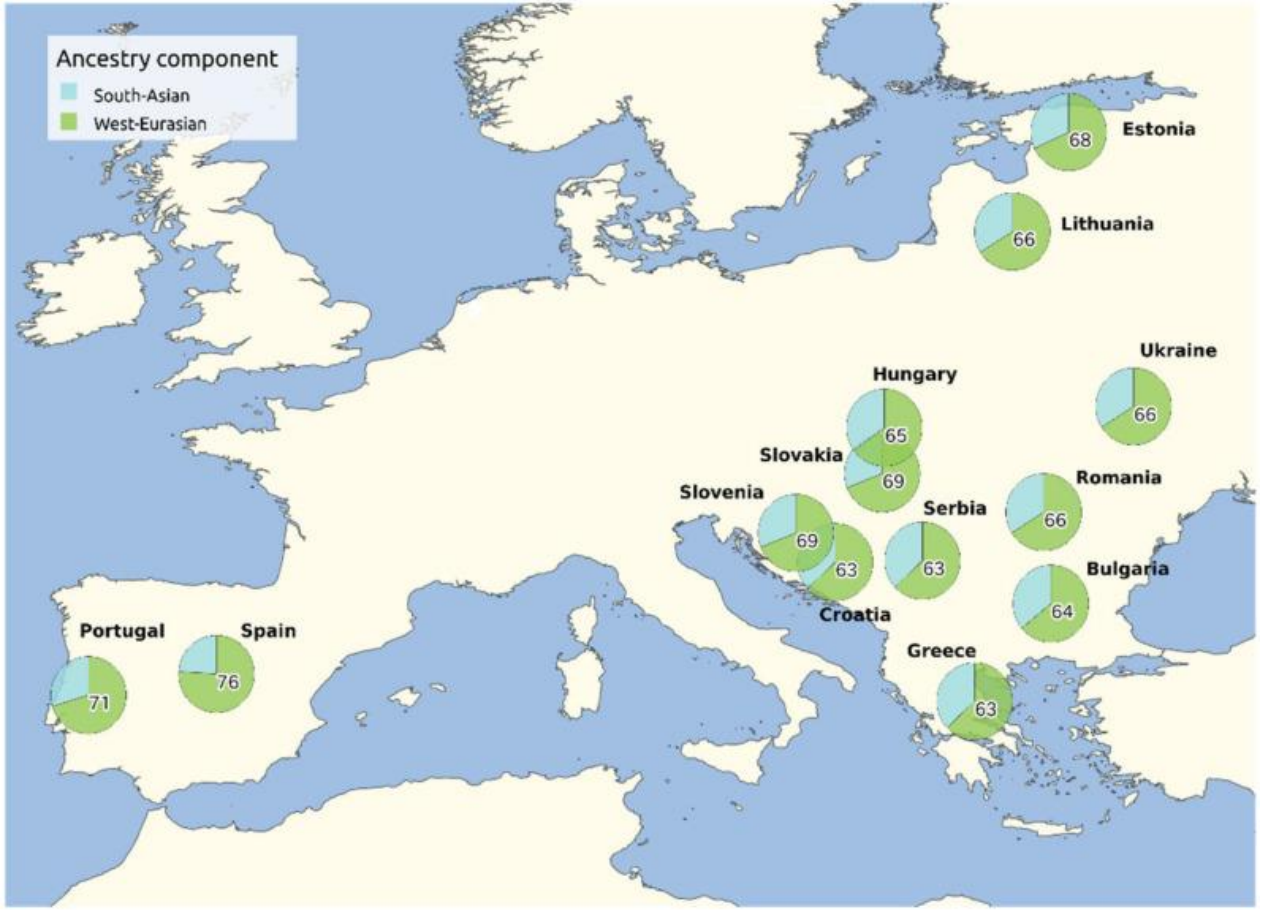
PREVALENCE OF MAJOR CHRONIC DISEASE

Roma communities appear to suffer higher rates of chronic disease (i.e. asthma, diabetes, cardiovascular disease, and hypertension) and the associated disability and limitations on daily activities.

A range of small scale studies highlight dramatically higher and more complex cases of chronic disease amongst Roma across a range of European Countries

Some evidence reports links between these higher rates of chronic disease, and higher prevalence of risk factors (e.g. diet, exercise, stress), poor access to and uptake of primary care and preventive health programmes among Roma.

GENETIC STRUCTURE OF ROMA POPULATIONS



- High **intra-group diversity** and **inter-group differentiation** across Europe.

Romanian Roma show:

- **~60–70% European admixture** (mostly Balkan and Romanian).
- **~30–40% South Asian ancestry**.
- Limited gene flow with non-Roma groups due to **endogamy** and **social isolation**.
- Genetic clustering corresponds to historical subgroups (e.g., *Kalderash*, *Lovari*, *Ursari*).

South Asian and West Eurasian ancestry components in Romani groups - **https://doi.org/ 10.3390/genes13112068**

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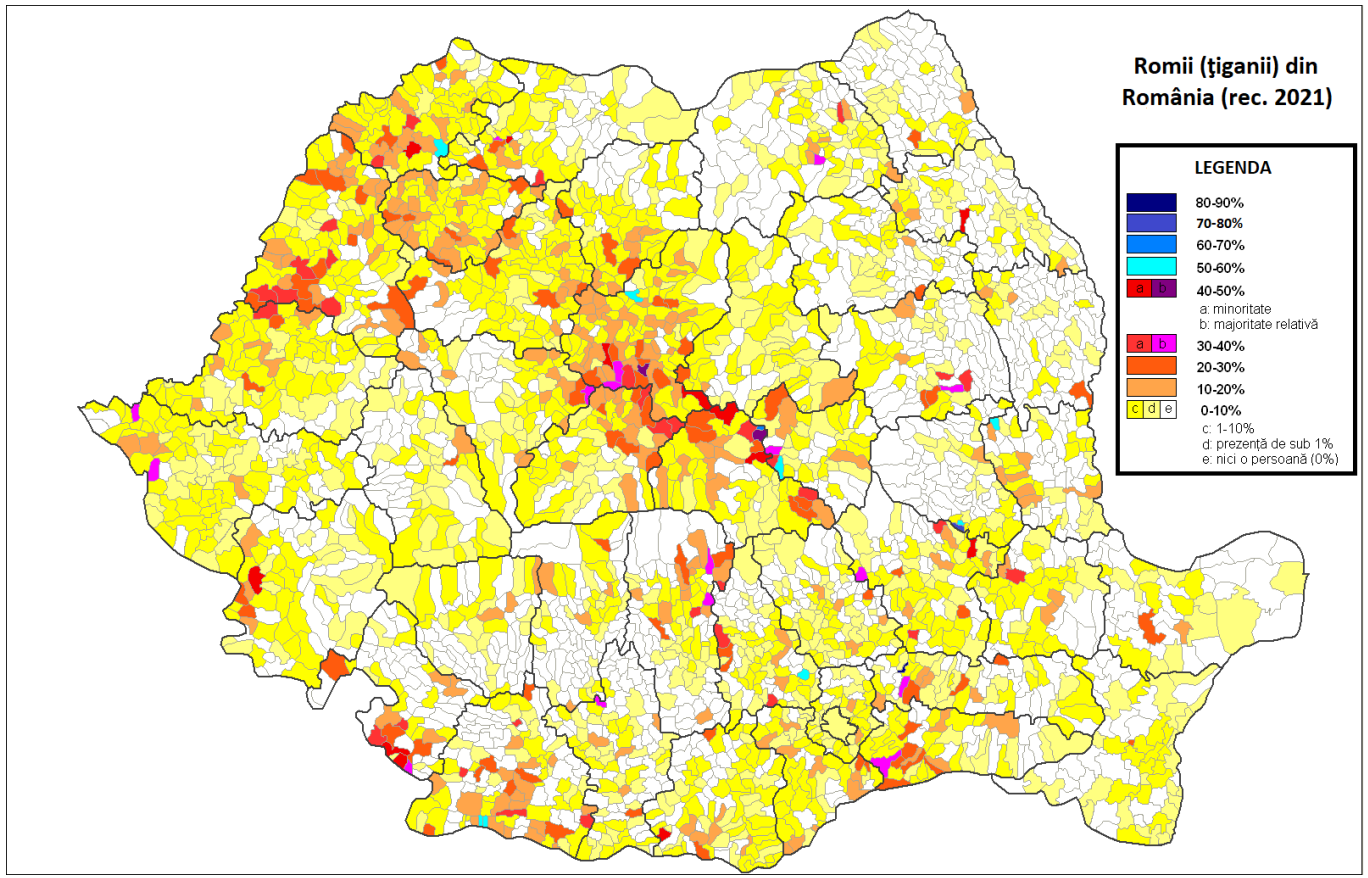
GENETIC DIVERSITY WITHIN ROMANIAN ROMA



The Romani minority in Romania by municipality - 2021

- Subgroups with different histories
- Genetic variation reflects migration waves
- Regional differences in allele frequencies

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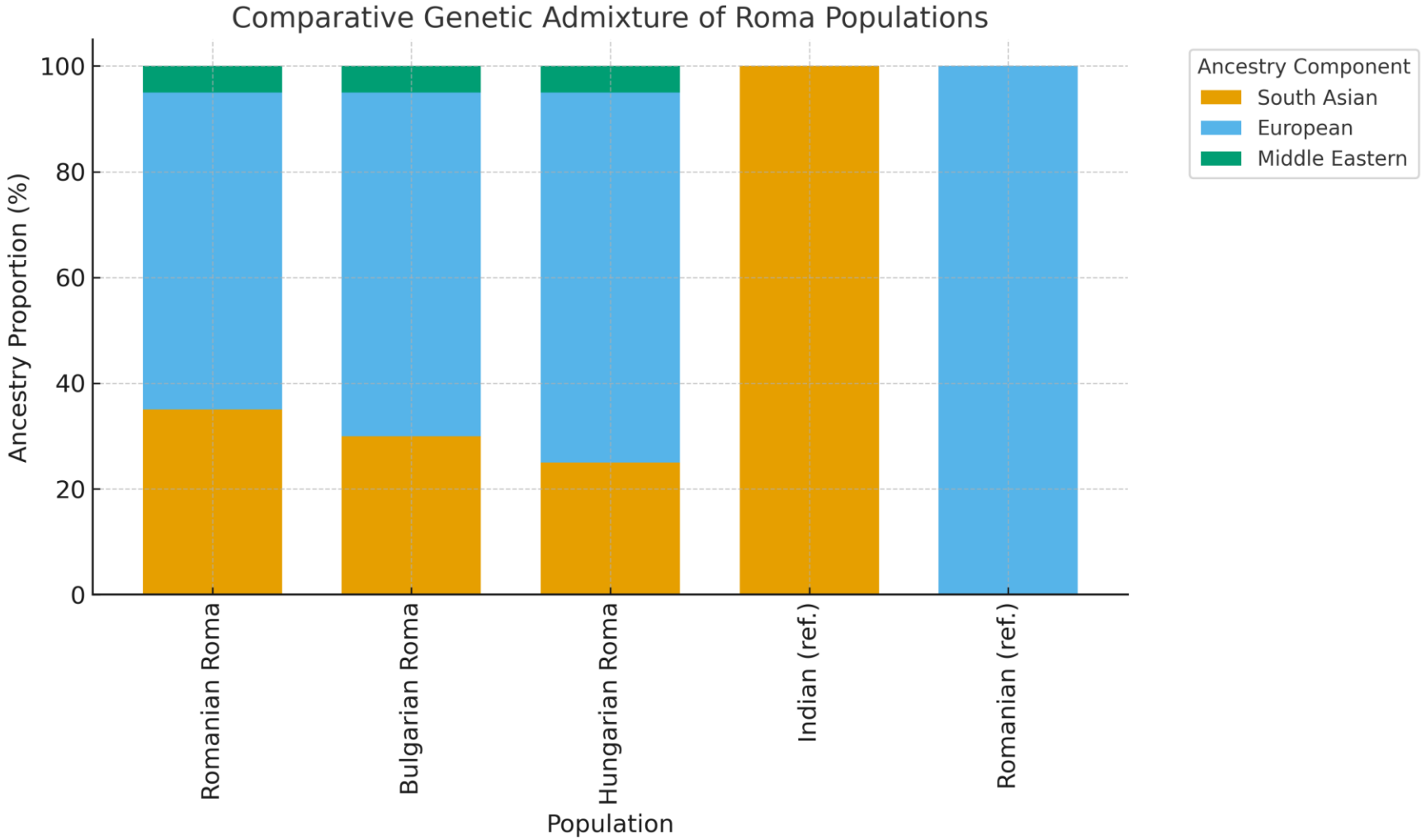
GENETIC ADMIXTURE



Comparative ancestry proportions (South Asian, European, Middle Eastern) for **Romanian, Bulgarian, and Hungarian Roma**, along with **Indian** and **Romanian reference populations**

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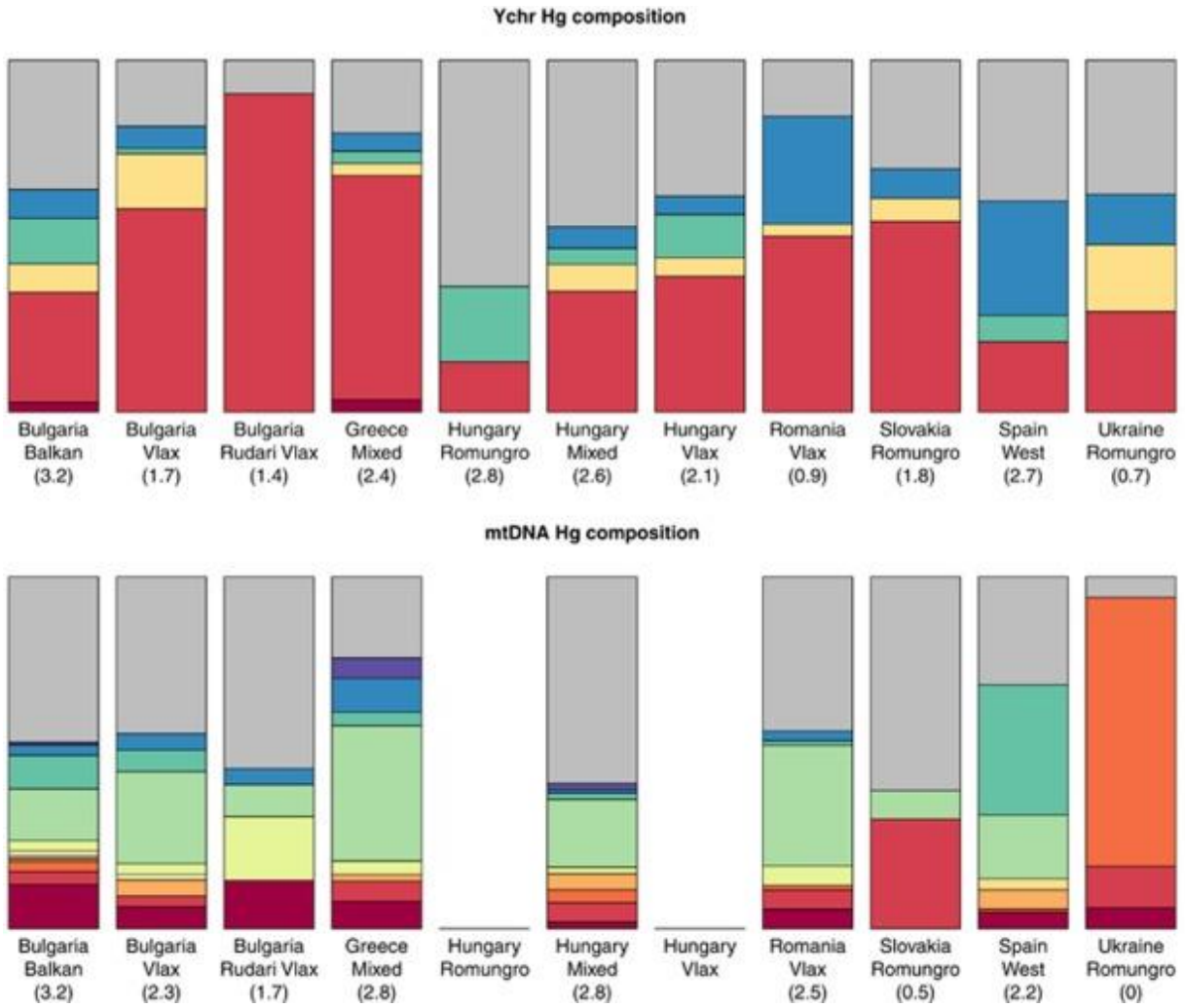
UNIPARENTAL MARKERS (MTDNA AND Y-CHROMOSOME)



(a) Y-chromosome and (b) mtDNA haplogroup frequencies corresponding to founder lineages in the European Roma populations. Non-founder haplogroups are grouped as 'others'. WIMP values for the group of founder lineages are shown in brackets at the bottom of each population sample.

- The genetic makeup of Romanian Roma is shaped differently by maternal and paternal lineages
- **Paternal (Y-chromosome) lineage:** South Asian lineages are more prevalent in paternal chromosomes, with the most common haplogroup being the South Asian M5a1b.
- **Maternal (mtDNA) lineage:** West Eurasian lineages are more common in maternal chromosomes. The most frequent maternal haplogroup is European H, which is also common in non-Roma Romanians, alongside other European haplogroups like U, T, K, and J.

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FACTORS INFLUENCING GENETIC DIVERSITY

Vincent van Gogh: The Caravans – Gypsy Camp near Arles (1888, oil on canvas)

Bottleneck and drift:

- Early migration involved a founder population that experienced a genetic bottleneck and subsequent drift, which significantly differentiated their uniparental genomes from the source populations and created a lower diversity in mtDNA compared to their host population.

Endogamy and consanguinity:

- Ongoing endogamy and consanguinity within the population have led to a higher frequency of certain recessive genetic disorders that are unique to the Roma.

Migration patterns:

- The history of migration and integration/segregation in different regions has further contributed to the genetic substructure seen within the Roma population across Europe.

IMPACT ON HEALTH AND MEDICAL GENETICS

Founder effects → high prevalence of certain **rare Mendelian diseases**.

Most founder mutations arose after the migration to Europe, but some retain **South Asian origins**.

Endogamy and bottlenecks amplified their frequency within specific Roma subgroups.

Underrepresentation in medical genetics studies → risk of **health inequality**.

Need for **targeted genetic screening** and **community health initiatives**.

These findings are crucial for **genetic screening, diagnostics, and community-specific healthcare strategies**

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FOUNDER MUTATIONS IN ROMA POPULATION

Founder Mutations in Roma Populations (with Romanian Focus)

Disease / Disorder	Gene	Mutation / Variant	Clinical Manifestation	Distribution
CCFDN	CTDP1	c.863+389C>T	Cataracts, dysmorphism, neuropa	Romanian & Bulgarian Roma
LGMD2C	SGCG	c.525delT	Muscle weakness, early onset	Bulgarian & Hungarian Roma
Non-syndromic Hearing Loss (DFN	GJB2	c.71G>A (p.W24X)	Congenital deafness	Romanian Roma
Neuronal Ceroid Lipofuscinosis (C	CLN6	c.316dupC	Neurodegeneration, seizures	Spanish & Romanian Roma
Primary Congenital Glaucoma (PC	CYP1B1	p.E229K, p.R368H	Blindness, high IOP	Eastern European Roma
Methylmalonic Acidemia (MMA)	MMACHC	c.271dupA	Metabolic crisis, growth failure	Czech & Slovak Roma
Beta-Thalassemia	HBB	IVS-I-110 (G>A)	Anemia, hemoglobinopathy	Mediterranean & Roma groups
Charcot–Marie–Tooth Disease Type	NDRG1	c.229C>T (p.R77X)	Peripheral neuropathy	Bulgarian & Romanian Roma

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LOCAL EXPERIENCE

Nomadic Romani family travelling in Moldavia, 1837

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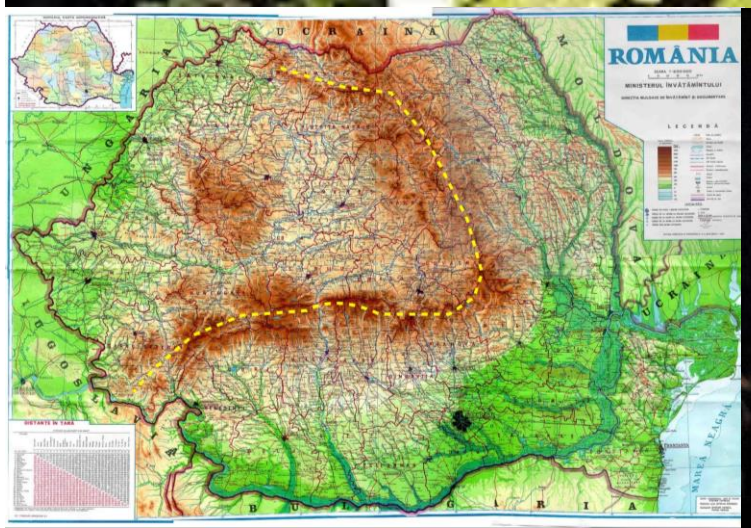
ROMANIA

- **LOCATION:** South-Eastern Europe, bordering: Bulgaria 608 Km, Hungary 443 Km, Moldova 450 Km, Serbia 476 Km, Ukraine (North) 362 Km, Ukraine (East) 169 Km
- **CAPITAL:** Bucharest
- **POPULATION:** 19+ Million (2019 EST.)
- **ETHNIC MAKE-UP:** Romanian 89.5%, Hungarian 6.6%, Roma 2.5%, Ukrainian 0.3%, German 0.3%, Russian 0.2%, Turkish 0.2%, Other 0.4%



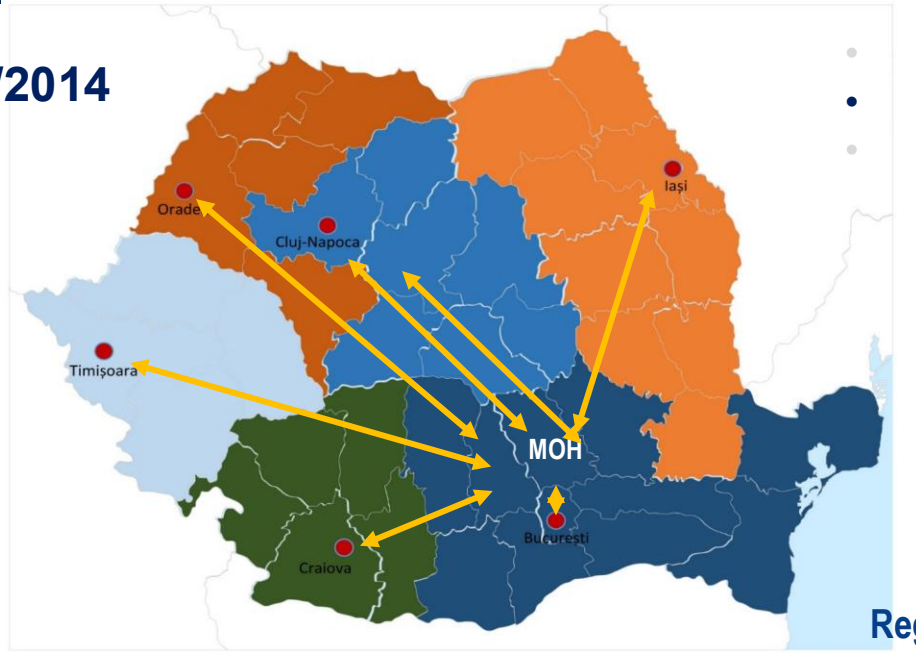
RARE GENETIC DISEASES IN ROMANIA

Romanian Network of Medical Genetics ?

7 Regional Center of Medical Genetics (CRGMs) ?

MINISTERUL SĂNĂTĂȚII

MOH 1358/2014



- Medical yard/compartment
- **GENETIC LABORATORY**
- Medical office - Outpatient clinic

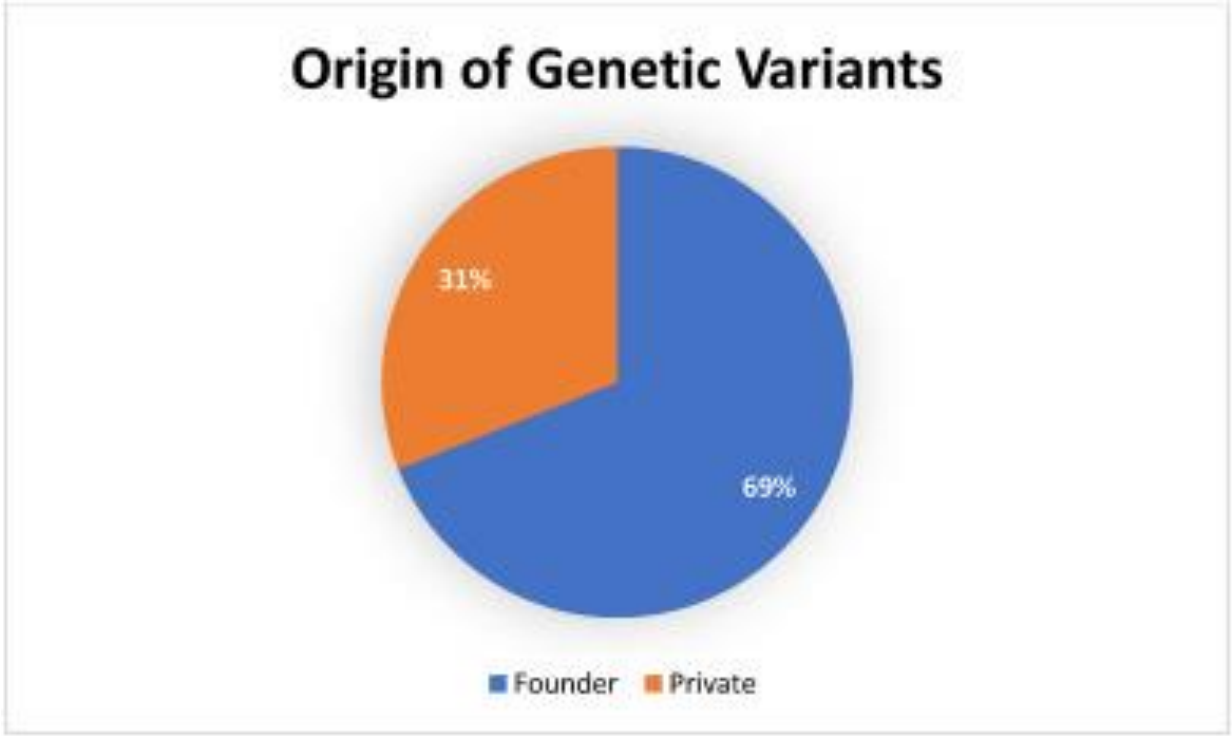
Regional Registry of Genetic Diseases

PARTICULARITIES OF GENETIC PATHOLOGIES DIAGNOSED AMONG ROMANIAN ROMA POPULATION

Genetic pathologies in the Romanian Roma population are distinct due to:

- founder effects and endogamy,

leading to higher frequencies of some inherited diseases like certain autosomal recessive neuropathies and muscular dystrophies.



GENETIC PATHOLOGIES DIAGNOSED AMONG ROMA POPULATION FROM SOUTHWEST OF ROMANIA

Gene	c.	p.	NM_	Inheritance	Phenotype
ABCA4	c.5917del	p.Val1973Ter	NM_000350.3	AR	Macular degeneration; Central retinitis pigmentosa
ACADM	c.985A>G	p.Lys329Glu	NM_000016.5	AR	MCAD deficiency
ANO10	c.1150_1151del	p.Leu384fs	NM_018075.5	AR	AR Cerebellar Ataxias (imbalance, unsteady gaits, incoordination, impaired speech, swallowing and eye movement)
ATP7B	c.3207C>A	p.His1069Gln	NM_000053.4	AR	Hepatic symptoms, arthralgia, anaemia, depression, dysarthria, failure to thrive, intellectual disability, jaundice, Kayser-Fleischer ring, proximal weakness in lower limbs, splenomegaly, weight loss
BBS5	c.226A>G	p.Ile76Val	NM_152384.3	AR	Polydactyly, kidney anomalies, genitourinary abnormalities, retinal dystrophy, obesity , developmental delay, intellectual disability
BBS12	c.1063C>T	p.Arg355*	NM_152618.3	AR	Polydactyly, kidney anomalies, genitourinary abnormalities, retinal dystrophy, obesity, developmental delay, intellectual disability
CEP290	c.384_387del	p.Asp128fs*	NM_025114.4	AR	Renal cystic dysplasia, CNS malformations, polydactyly, hepatic developmental defects, pulmonary hypoplasia
CLCN1	c.562+1G>C		NM_000083.2	AR	Congenital myotonia
CYP24A1	c.989C>T	p.Thr330Met	NM_000782.5	AR	Failure to thrive, muscle hypotonia, hypercalcaemia
CYP24A1	c.428_430delAAG	p.Glu143del	NM_000782.5	AR	Failure to thrive, muscle hypotonia, hypercalcaemia
FAR1	c.830C>A	p.Pro277His	NM_032228.5	AR	Microcephaly, developmental delay, seizures, hypotonia, cerebellar atrophy, spasticity, intellectual disability, cataracts, short stature
FRRS1L	c.775C>T	p.Arg259Cys	NM_014334.3	AR	Abnormal CNS myelination; Ataxia; Developmental regression; Febrile seizures; Global developmental delay; Hypsarrhythmia; Optic atrophy; Progressive neurologic deterioration; Psychomotor retardation; Retinal atrophy; Seizures, intellectual disability
GLB1	c.176G>A	p.Arg59His	NM_000404.3	AR	Early onset CNS involvement, skeletal dysplasia, ocular anomalies, visceromegaly, progression to death, Dilated cardiomyopathy; Hepatomegaly; Joint stiffness; Developmental delay, Intellectual disability, Hearing impairment
HINT1	c.110G>C	p.Arg37Pro	NM_005340.7	AR	Muscle weakness and atrophy; Axonal neuropathy; Impaired gait
HK1	c.278G>A	p.Arg93Gln	NM_033496.2	AR	Haemolytic anaemia, epileptic encephalopathy and dev delay
KCNQ1	c.604G>A	p.Asp202Asn	NM_000218.2	AR	Sensorineural hearing impairment, prolonged QT interval, arrythmia, syncope, seizures
LAMB3	c.1133-22G>A		NM_000228.3	AR	Junctional Epidermolysis Bullosa
NDRG1	c.422C>T	p.Arg148Ter	NM_006096.3	AR	Distal limb weakness and atrophy, gait disorder, deafness, hand and feet deformities
NDST1	c.1831G>A	p.Gly611Ser	NM_001543.5	AR	Delayed psychomotor development; Hypotonia;Neuropathy, intellectual disability
PTS	c.84-3C>G		NM_000317.2	AR	Hypotonia, opisthotonus, ataxia, chorea, global developmental delay, intellectual disability, seizures
SLC37A4	c.712G>C	p.Gly238Arg	ENST00000357590.5	AR	Glycogen and fat storage in liver ? Kidneys-hepatomegaly and nephromegaly. Neutropenia and severe hypoglycemia.
SPG7	c.233T>A	p.Leu78Ter	NM_003119.4	HD/AR	Scoliosis; Ataxic gait; Nystagmus; Intellectual disability
TK2	c.644T>C	p.Leu215Pro	NM_004614.4	AR	Respiratory insufficiency; Limb muscle weakness; Muscle atrophy, hypotonia, motor deterioration, developmental regression, failure to thrive, seizures
TK2	c.668G>T	p.Gly223Val	NM_004614.4	AR	Respiratory insufficiency; Limb muscle weakness; Muscle atrophy, hypotonia, motor deterioration, developmental regression, failure to thrive, seizures,

Quinn S, Walsh N, Streata I, Ververi A, Kulshrestha S, Puri RD, Riza AL, Walsh A, Gorman K, Crushell E, Green A, Kenny J, Lynch SA. Catalogue of inherited autosomal recessive disorders found amongst the Roma population of Europe. Eur J Med Genet. 2025

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ETHICAL AND SOCIAL CONSIDERATIONS IN GENETIC COUNSELLING

Gypsy Camp **by Jan van de Venne, depicting a 17th century Romani encampment**

- Importance of **avoiding stigmatization** in genetic reporting.
- Need for **community engagement** and **informed consent**.
- Genetics should support **health equity**, not reinforce stereotypes.

Gypsy Woman with Baby **by Amedeo Modigliani, 1919**

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SUMMARY

A Romani family

- Roma populations (including Romanian Roma) = a **genetically distinct diverse** group.

- Genetic signatures reflect:
  - Indian origin
  - European admixture
  - Bottlenecks and founder effects
  - Implications for both **anthropological understanding** and **medical genetics.**

A Gypsy Dance in the Gardens of Alcázar by Alfred Dehodencq, 1851

THANK YOU!

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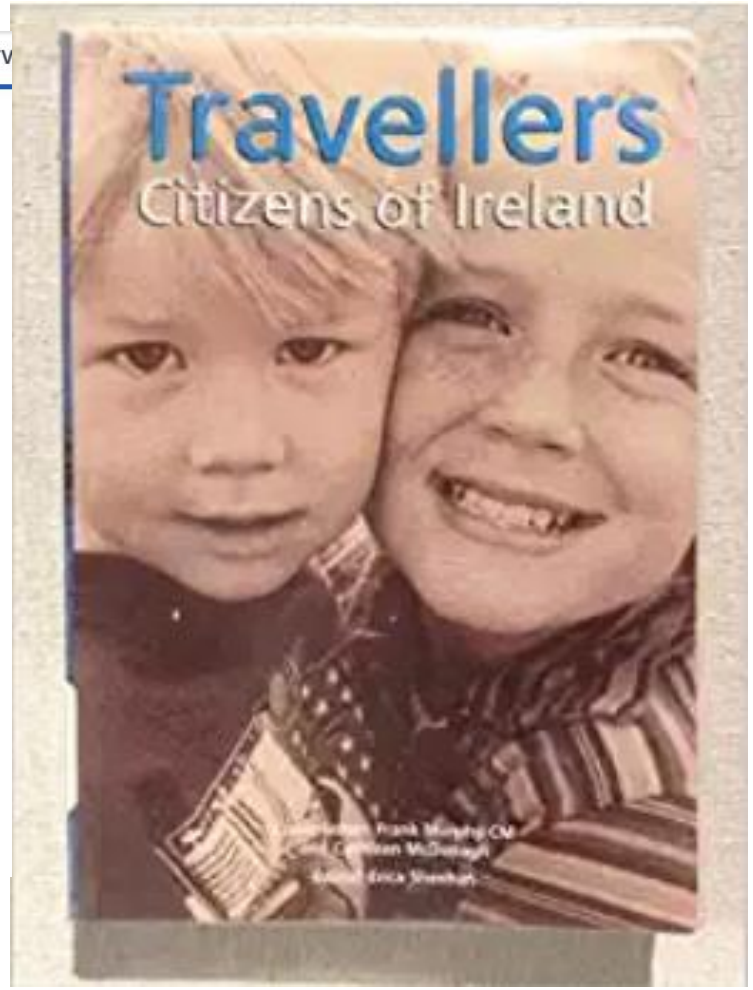
ITHACA

Topic 4 - The Irish Travellers

Sally Ann Lynch, CHI Crumlin & Temple Street, Dublin, Rep of Ireland

Ethnic minority endogamous population indigenous to island of Ireland



Ethnicity recorded in health care records in RoI

Frank McDonagh, Cathleen Murphy (2000)

Europe

Main article: Ethnic groups in Europe

See also: Genetic history of Europe and Category:Indigenous peoples of Europe

Various ethnic groups have lived in Europe for millennia. However, the UN recognizes very few Indigenous populations within Europe, which are confined to the far north and far east of the continent.

Notable Indigenous minority populations in Europe that are recognized by the UN include the Sámi peoples of northern Norway, Sweden, and Finland and northwestern Russia (in an area also referred to as Sápmi); the Uralic Nenets, Samoyed, and Komi peoples of northern Russia;[150] the Circassians of southern Russia and the North Caucasus; the Crimean Tatars, Krymchaks, and Crimean Karaites of Crimea in Ukraine; the Basques of Basque Country, Spain and southern France; the Sorbs of Germany and Poland, the Irish Travellers of the island of Ireland,[151][152] and the Sardinians of Sardinia.[153][154]

A Maya family in the hamlet of Palzulzun, Guatemala, 1993

Peoples are usually described as "Indigenous" when they maintain traditions or other aspects of an early culture that is associated with the first inhabitants of a given region.[10] Not all Indigenous peoples share this characteristic, as many have adopted substantial elements of a colonizing culture, such as dress, religion or language. Indigenous peoples may be settled in a given region (sedentary), exhibit a nomadic lifestyle across a large territory, or be resettled, but they are generally historically associated with a specific territory on which they depend. Indigenous societies are found in every inhabited climate zone and continent of the world except Antarctica.[11] There are approximately five thousand Indigenous nations throughout the world.[12]

Indigenous peoples' homelands have historically been colonized by larger ethnic groups, who justified colonization with beliefs of racial and religious superiority, land use or economic opportunity.[13] Thousands of Indigenous nations throughout the world currently live in countries where they are not a majority ethnic group.[14] Indigenous peoples continue to face threats to their sovereignty, economic well-being, languages, ways of knowing, and access

Semantics: Travellers are a population, not a community
Its Travellers with a capital T!

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If Travellers are Irish ethnically- When did they diverge?

- DNA variants are seen in Irish non-Travellers
- Travellers diverged from non-Trav population centuries ago-long before potato famine 1840's
- Nomadic culture-Illiteracy –paucity of written records
- ~at least 360 years ago ? 12th century (Tincaid=tinman)

SCIENTIFIC REPORTS

OPEN

Received: 23 August 2016
Accepted: 04 January 2017
Published: 09 February 2017

Genomic insights into the population structure and history of the Irish Travellers

Edmund Gilbert[1], Shai Carmi[2], Sean Ennis[3], James F. Wilson[4,5,*] & Gianpiero L. Cavalleri[1,*]

The Irish Travellers are a population with a history of nomadism; consanguineous unions are common and they are socially isolated from the surrounding, 'settled' Irish people. Low-resolution genetic analysis suggests a common Irish origin between the settled and the Traveller populations. What is not known, however, is the extent of population structure within the Irish Travellers, the time of divergence from the general Irish population, or the extent of autozygosity. Using a sample of 50 Irish Travellers, 143 European Roma, 2232 settled Irish, 2039 British and 6255 European or world-wide individuals, we demonstrate evidence for population substructure within the Irish Traveller population, and estimate a time of divergence before the Great Famine of 1845–1852. We quantify the high levels of autozygosity, which are comparable to levels previously described in Orcadian 1st/2nd cousin offspring, and finally show the Irish Traveller population has no particular genetic links to the European Roma. The levels of autozygosity and distinct Irish origins have implications for disease mapping within Ireland, while the population structure and divergence inform on social history.

European Reference Networks ITHACA

Clans- surnames & disorders map geographical regions of Ireland

The number of Irish Travellers living in the State and counted in Census 2022 was 32,949, an increase of 6% from 30,987 in the 2016 census. Irish Travellers make up less than 1% of the population so, for comparison purposes, it can be helpful to use rates per 1,000 of the population. This shows that in Census 2022, six out of 1,000 people in the State were Irish Travellers. The proportion of Irish Travellers in the population varied from county to county.

- In Galway City, 21 out of every 1,000 people were Irish Travellers, in Longford, the rate was 20 per 1,000 of the population and in Offaly, it was 14 per 1,000.
- Dún Laoghaire-Rathdown had the lowest number of Irish Travellers per 1,000 of the population with just under two Irish Travellers for every 1,000 people.
- In Kildare and Dublin City, there were just under four Irish Travellers for every 1,000 people.
- The Irish Traveller population increased in most counties, the largest rise being recorded in Offaly, up 30% to 1,174.
- The Traveller population also increased by more than 200 in Cork (up 11% to 2,376), Fingal (up 17% to 1,545) and Tipperary (up 17% to 1,434).
- There were drops in the number of Irish Travellers in some counties; the largest were recorded in Longford (down 13% to 913) and South Dublin (down 12% to 1,943).

(1,770 in Northern Ireland- 0.1%)

www.cso.ie

Irish Travellers

- Most live in houses but 8% nomadic
- No genetic relationship to the Roma
- How many live in European mainland/UK/US?
- 27 yrs average age of a Traveller compared to 39 yrs 2022 www.cso.ie

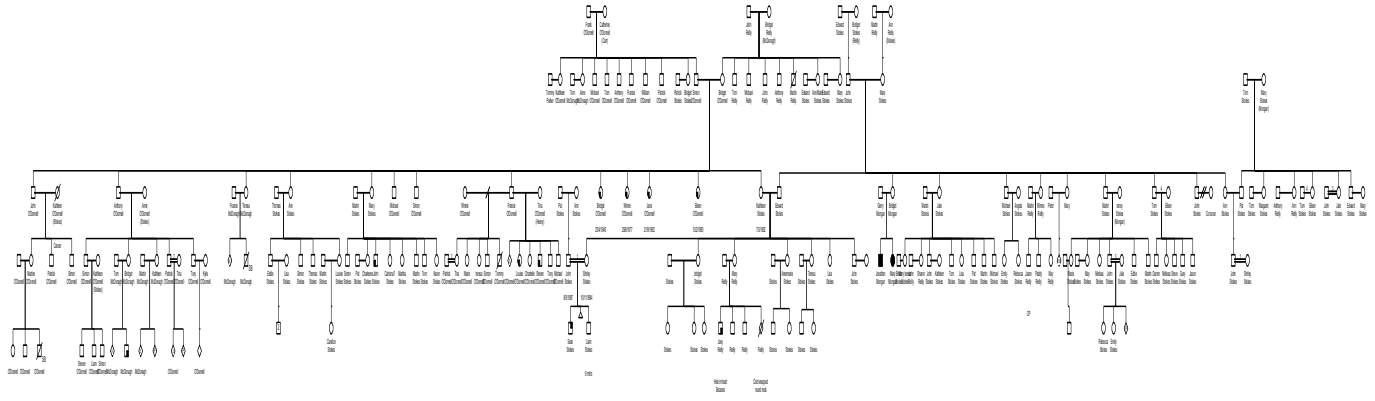
Beside Guinness museum in Dublin

2022 census www.cso.ie

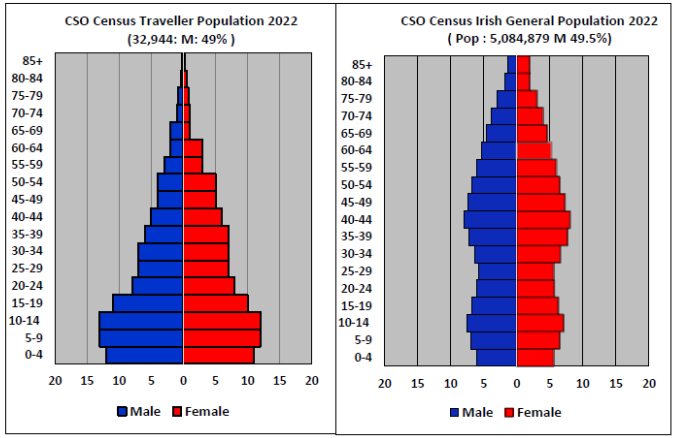
Highest Level of Education Completed	UNIT	Total persons
Total education ceased and not ceased	Number	20969
No formal education	Number	2761
Primary	Number	4043
Lower secondary	Number	3362
Upper secondary	Number	1531
Technical/vocational	Number	387
Doctorate (PhD)	Number	16
Economic status - total at school, university, etc.	Number	2777
Economic status - other	Number	3622
Advanced certificate/completed apprenticeship	Number	149
Higher certificate	Number	140
Ordinary bachelor degree/professional qualification or both	Number	114
Honours bachelor degree/professional qualification or both	Number	115
Postgraduate diploma or degree	Number	67
Not stated	Number	1885

Traveller family tree-demographics differ
How many first cousins do you have?

80 first cousins (I have 24)



Traveller women average life span 50 years



- Travellers continue to have a population pyramid reflective of a developing country with higher fertility, higher mortality across all ages and genders and shorter life expectancy.
- The data for Travellers surviving to over age 65 is improving since 2016 when 3% were over 65 to 4.2% in 2022 but the gap between Travellers and the general population continues to widen as 11% of the general population were aged over 65 in 2016 and they are now 15% in 2022.

Number of Travellers enumerated in CSO Census 2022 = 32,949

This is a 6% increase in Traveller population since 2016

www.cso.ie

202 individuals in 4 generations, in total 8 surnames= 25.3 people per surname. Clans marry within clan,

Disorders cluster in specific clans/geography

Lynch family 98 individuals; 9 surnames in 4th generation; 16 surnames in 3rd generation, 10 surnames 2nd, 8 in first =43 in total= 2.3 people per surname

European Reference Networks ITHACA

Endogamous populations-rule of thumb

- marry within their (wider) community
- [Roma, Jewish, nomadic Middle-Ea populations]
- tend to have large families
- Consanguinity occurs in some..
- ↑ risk autosomal recessive disorders
- AR risk ↑ the smaller the populatior

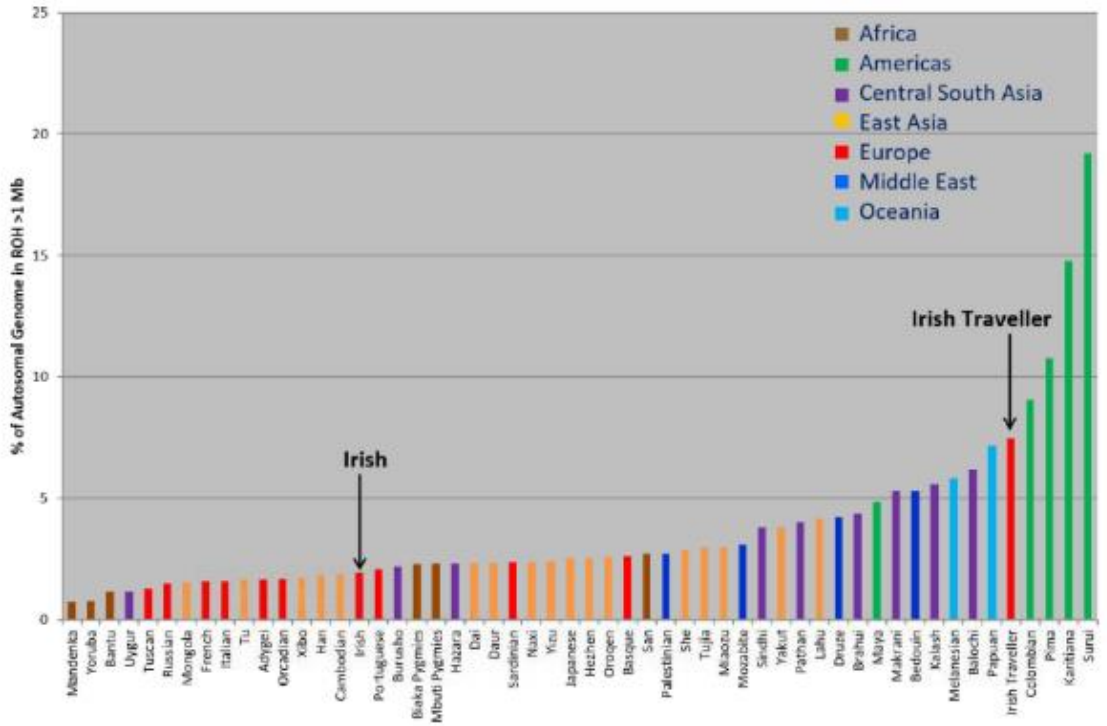


Figure 1 SNP-based comparison of the percentage of the autosomal genome located in a run of homozygosity (ROH) >1 Mb. Populations analysed include the Irish Travellers, the general Irish population and 51 populations from the HGDP dataset. The average level of homozygosity in the Irish Traveller population was found to be 8%, compared with 2% in the general Irish population.

Lynch SA, *et al*. *J Med Genet* 2018;**0**:1–7. doi:10.1136/jmedgenet-2017-104974

European Reference Networks ITHACA

Traveller Marriages

- occur at young age (getting later). Having children very important to Traveller culture
- 39% first cousin- 71% cousin marriage M Flynn 1997 Irish Med J
- Family size now much smaller (~4-6)
- Consanguineous marriage=favoured custom 10-20% world-regions with combined popn 720 million people)
- first cousin marriages not the norm in Europe- prejudice is strong
- if seeing- child has a genetic disorder re-enforcing beliefs about 1st cousin marriage
- Mistrust of medical/nurse professionals

Travellers & health care professionals

- Privacy is important
- need to know basis
- secretive about family information
- pedigree can change on 2nd attempt
- repetitive first names and surnames
- very difficult to link families
- Avoid “are you first cousins”

Diagnostics
Original Article

Journal of Medical Genetics 2018

PDF

Catalogue of inherited disorders found among the Irish Traveller population

Sally Ann Lynch[1, 2], Ellen Crushell[2, 3], Deborah M Lambert[1], Niall Byrne[1], Kathleen Gorman[2, 4], Mary D King[2, 4], Andrew Green[2], Siobhan O'Sullivan[5], Fiona Browne[6], Joanne Hughes[3], Ina Knerr[3], Ahmad A Monavari[3], Melanie Cotter[7], Vivienne P M McConnell[8], Bronwyn Kerr[9], Simon A Jones[9], Catriona Keenan[10], Nuala Murphy[11], Declan Cody[12], Sean Ennis[2], Jackie Turner[1], Alan D Irvine[6, 13], Jillian Casey[2]

Author affiliations +

Ref 6-20- not explicitly Travellers

Abstract

Background Irish Travellers are an endogamous, nomadic, ethnic minority population mostly resident on the island of Ireland with smaller populations in Europe and the USA. High levels of consanguinity result in many rare autosomal recessive disorders. Due to founder effects and endogamy, most recessive disorders are caused by specific homozygous mutations unique to this population. Key clinicians and scientists with experience in managing rare disorders seen in this population have developed a de facto advisory service on differential diagnoses to consider when faced with specific clinical scenarios.

Objective(s) To catalogue all known inherited disorders found in the Irish Traveller population.

Methods We performed detailed literature and database searches to identify relevant publications and the disease mutations of known genetic disorders found in Irish Travellers.

Results We identified 104 genetic disorders: 90 inherited in an autosomal recessive manner; 13 autosomal dominant and one a recurring chromosomal duplication.

Conclusion We have collated our experience of inherited disorders found in the Irish Traveller population to make it publically available through this publication to facilitate a targeted genetic approach to diagnostics in this ethnic group.

http://dx.doi.org/10.1136/jmedgenet-2017-104974

Cataloguing inherited genetic disorders should improve (early) diagnoses & outcome of rare disorders-mo autosomal recessive

Home › European Journal of Pediatrics › Article

An approach to recognising and identifying metabolic presentations in the paediatric Irish Traveller population

Review | Published: 14 November 2022

Volume 182, pages 31–40, (2023) Cite this article

E. B. Forman, S. A. Lynch, I. Knerr, A. Monavari, J. Hughes, R. Boruah, A. Green & E. Crushell

Review article

A perinatal approach to genetic disorders in Irish Travellers: A review

Fionnuala Mone[a], Fionnuala M. McAuliffe[a], Sally Ann Lynch[b,c,*]

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[b] National Rare Disease Office, Mater Misericordiae University Hospital, Dublin 7, Ireland
[c] UCD Academic Centre on Rare Diseases, University College Dublin, Dublin 4 Ireland

Learn the (ultra) rare disorders in your populations & publish them

Table 2 (continued)

Age of onset	Condition	Gene	OMIM	Observed occurrence	Clinical features	Other tests to consider
Infantile/ later childhood						
	Phenylketonuria	*PAH*	612349	F	Intellectual disability, seizures, developmental delay, behaviour problems, psychiatric disorders, lighter hair and skin. In DHPR deficiency – movement disorder also.	Elevated phenylalanine usually det on newborn screening. Serum amino acids. Pterin analysis to rule out DHPR.
	DHPR deficiency	*QDPR*	261630			
	Hurler syndrome	*IDUA*	607014	F	Developmental delay/regression, hepatosplenomegaly, gibbus deformity, frontal bossing, hearing loss, language delay, corneal clouding and carpal tunnel syndrome.	Urine glycosaminoglycans, lysosoi enzyme testing.
	Medium chain acyl CoA dehydrogenase deficiency	*ACADM*	607008	F	Episodes of hypoglycaemia associated with lethargy, vomiting, seizures, breathing difficulties, liver failure, coma and sometimes sudden death.	Acylcarnitine profile.
	Glutaric aciduria type I	*GCDH*	608801	F	Initially normal with macrocephaly, deterioration in infancy with hypotonia and dystonia and abnormal movements.	Urine organic acids, MRI brain, acylcarnitine profile.
	Leigh syndrome	*COX15 / ECHS1 / SURF1*	256000	P/P/F	Vomiting, diarrhoea, dysphagia, failure to thrive, hypotonia, dystonia, rigidity, ataxia and seizures.	MRI brain with MRS, serum lacta
	Infantile liver failure—multisystem involvement	*LARS*	615438	C	Episodic fever related acute liver failure and seizures.	Liver function tests, albumin, FBC LARS1 mutation analysis.
	Byler disease	*ATP8B1*	211600	C	Early onset of loose, foul-smelling stools, conjugated jaundice, hepatosplenomegaly, impaired growth with short stature.	Low calcium, high phosphorus, hi bilirubin.
	Alpers syndrome	*POLG*	203700	P	Seizures (epilepsy partialis continua) with neurodegeneration, regression, neuropathy, movement disorder and liver failure.	MRI brain,EEG, liver function test
	Mitochondrial complex II deficiency	*SDHD*	602690	P	Progressive loss of skills and seizures. Leigh like phenotype.	Muscle biopsy, serum lactate.
	Glycogen storage disease III/V (McArdle)	*AGL* *PYGM*	610860 613741	C/F	Hepatomegaly, hypoglycaemia, growth retardation, muscle weakness and cardiac involvement.	glucose, ketones (fasting), lipids, creatinine kinase, liver function.
	Wilson's disease	*ATP7B*	277900	C	Liver failure—tiredness, bleeding and hepatic encephalopathy with neuropsychiatric symptoms and parkinsonism.	Copper, Caeruloplasmin. Ophthalr review.

confirmation or exclusion of diagnoses as it allows targeted screening for the specific mutation. The aim of this review is to act below [Fig. 1], as are multisystem disorders [Table 1]. Information is also provided on the occurrence of such genetic mutations

Table 1
Traveller syndromes presenting as a multisystem disorder on antenatal ultrasound (FGR= Fetal growth restriction; Observed occurrence: P = Private mutations, seen in one nuclear family; C = multiple affected individuals within one Clan; F = Founder mutations, seen in unrelated families).

	FGR	Hydrops	Brain	Cranio/ Facial	Cardiac	Thorax	Uro-genital	Musculo-Skeletal	Observed occurence
Beaulieu-Boycott-Innes syndrome *THOC6*			x				x		P
Colobomatous microanopthalmia (MCOPCB) and Matthew Woods syndrome *STRA6*	x		x	x	x	x	X	x	F
Deafness, onychodystrophy, osteodystrophy, mental retardation, and seizures (DOOR) syndrome *TBC1D24*			x		x		x		P
Fanconi anaemia of complementation group A or J *FANCA* and *BRIP1*	x		x	x	x		X	x	F/P
Fraser syndrome *FREM2*			x	x	x	x	X	x	C
I-cell disease mucolipidosis II *GNPTAB*	x	x			x			x	F
Meckel syndrome *unknown*			x	x	x	x	X	x	P
NEK9 related lethal skeletal dysplasia[17] *NEK9*				x	x	x		x	F
Neu-Laxova syndrome *unknown*	x		x	x		x		x	P
Van Maldergem Syndrome 1 *DCHS1*			x	x			x	x	P
Walker-Warburg syndrome *POMT1*			x	x					F

European Reference Networks ITHACA

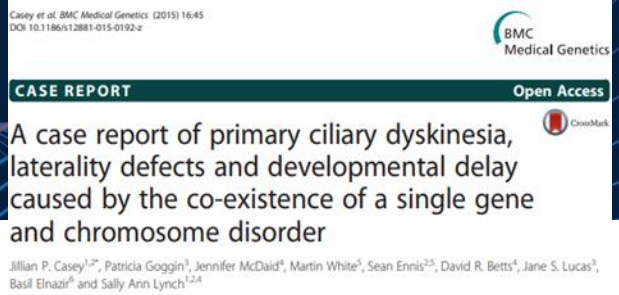
Multicenter Study > Arch Dis Child. 2009 Jan;94(1):52-4. doi: 10.1136/adc.2007.135772. Epub 2008 May 7.

Incidence and prevalence of mucopolysaccharidosis type 1 in the Irish republic

A M Murphy [1], D Lambert, E P Treacy, A O'Meara, S A Lynch

Affiliations + expand

PMID: 18463126 DOI: 10.1136/adc.2007.135772



Casey et al. BMC Medical Genetics (2015) 16:45
DOI 10.1186/s12881-015-0192-z

BMC Medical Genetics

CASE REPORT Open Access

A case report of primary ciliary dyskinesia, laterality defects and developmental delay caused by the co-existence of a single gene and chromosome disorder

Jillian P. Casey[1,2*], Patricia Goggin[3], Jennifer McDaid[4], Martin White[5], Sean Ennis[2,5], David R. Betts[4], Jane S. Lucas[3], Basil Elnazir[6] and Sally Ann Lynch[1,2,4]

Disease	Carrier freq in Trav	Carrier frequency in Irish non-Travellers	Ref
Hurler syndrome	1/10	1/81	31
Galactosemia	1/11	1/107	32-35
I cell disease	1/15	1/512	36

Linkage disequilibrium

Chromosomal locus	Disorders	Number of individuals	Number of Families	Ref
11q13.1	McArdle Disease	11	4	50
	Microcephaly			
9p13.3/9q21.11	Galactosemia	11	7	60
	Friedreich Ataxia			
17q	Primary Ciliary Dyskinesia with laterality defect	4	1	26
	17q duplication			

European Reference Networks ITHACA

Koren Callanan, David Evans, Mary Syron Dec 2002 (Western Health Board)

12% of parents had one or more stillbirths
8% had suffered the death of a child < 1 year
6% had suffered the death of a child > 1 year.
9% of parents had child with metabolic disorder
5% a child with a disability.

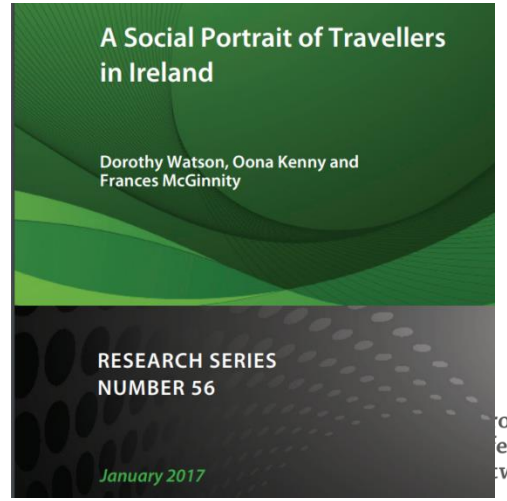
Q10. (a) Have any of your children ever suffered with the following health problems? (Read FROM list)

	Yes	No	Don't Know
Child with Hurlers Syndrome	1	2	3
Child with a disability	1	2	3
Child with galactocaemia	1	2	3
Child with a chest infection	1	2	3
Child with vomiting and diarrohea (gastroenteritis)	1	2	3
Child with early blindness (retinitispigmentosa)	1	2	3
Child with deafness	1	2	3
Child that has problems with bones that break easily (Brittle Bone disease)	1	2	3
Other health problems (please specify)	1	2	3

Lynch SA et al. 2018 J Med Genet
27 (26%) -associated with early childhood death
16 (15.4%) -adult onset conditions
5 (4.8%) - associated with fetal loss.
9 (37.5%) -congenital anomalies
39 (37.5%) -intellectual disability
34 (32.7%) -metabolic disorder
33 (31.7%) -neurological phenotype (aside from intellectual disability)
7 (6.7%) associated with cancer susceptibility.
Now 145 disorders

Health stats: Room to improve?

- 2 DoH reports ESRI 2017 –DoH 1987 stats had hardly improved
- Child mortality up to age 10 has been found to be 10 times that of the population as a whole.
- ~Travellers die ~15 years earlier than general population. Only 1/ 10 of the Traveller population is >40 years & only 1/100 is >65
- The Irish Sudden Infant Death Association 1999- rate of (SIDS) among Travellers >12 times greater than the settled population
- Worst health stats in the EU



What is true risk of having a child with a problem in IT population?

- No one knows
- Prospective study required- blocked in past with ethics
- Murphy AM –prospective review over 6mths 28/84 (33%) of referrals Travellers. Uls Med Journal 2008 ISHG abstract
- Ethical barriers-?Less now ethnicity status- March 2017

Lancet. 2013 Oct 19;382(9901):1350-9. doi: 10.1016/S0140-6736(13)61132-0. Epub 2013 Jul 4.

Risk factors for congenital anomaly in a multiethnic birth cohort: an analysis of the Born in Bradford study

Eamonn Sheridan [1], John Wright, Neil Small, Peter C Corry, Sam Oddie, Catherine Whibley, Emily S Petherick, Teena Malik, Nicole Pawson, Patricia A McKinney, Roger C Parslow

Affiliations + expand

PMID: 23830354 DOI: 10.1016/S0140-6736(13)61132-0

Abstract

Background: Congenital anomalies are a leading cause of infant death and disability and their incidence varies between ethnic groups in the UK. Rates of infant death are highest in children of Pakistani origin, and congenital anomalies are the most common cause of death in children younger than 12 in this ethnic group. We investigated the incidence of congenital anomalies in a large multiethnic birth cohort to identify the causes of the excess of congenital anomalies in this community.

Findings: Of 11,396 babies for whom questionnaire data were available, 386 (3%) had a congenital anomaly. Rates for congenital anomaly were 305·74 per 10,000 livebirths, compared with a national rate of 165·90 per 10,000. The risk was greater for mothers of Pakistani origin than for those of white British origin (univariate RR 1·96, 95% CI 1·56-2·46). Overall, 2013 (18%) babies were the offspring of first-cousin unions. These babies were mainly of Pakistani origin--1922 (37%) of 5127 babies of Pakistani origin had parents in first-cousin unions. Consanguinity was associated with a doubling of risk for congenital anomaly (multivariate RR 2·19, 95% CI 1·67-2·85); we noted no association with increasing deprivation. 31% of all anomalies in children of Pakistani origin could be attributed to consanguinity. We noted a similar increase in risk for mothers of white British origin older than 34 years (multivariate RR 1·83, 95% CI 1·14-3·00). Maternal education to degree level was protective (0·53, 95% CI 0·38-0·75), irrespective of ethnic origin.

Interpretation: Consanguinity is a major risk factor for congenital anomaly. The risk remains even after adjustment for deprivation, and accounts for almost a third of anomalies in babies of Pakistani origin. High levels of educational attainment are associated with reduced risk in all ethnic groups. Our findings will be valuable in health promotion and public health, and to those commissioning antenatal, paediatric, and clinical genetic services. Sensitive advice about the risks should be provided to communities at increased risk, and to couples in consanguineous unions, to assist in reproductive decision making.

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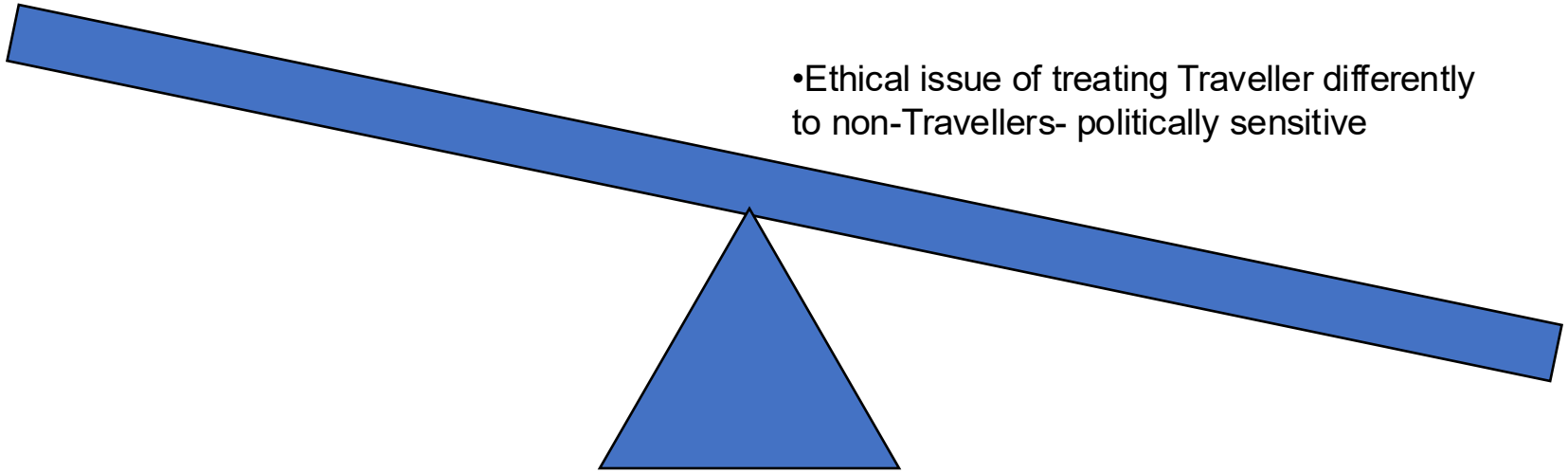
What is stopping us from offering screening to this population? -paralysis

Right to latest information about new tests



1) They are not asking; they have right to take risk
2) Resources don't allow it & political will not there
3) Travellers are individuals too so we cannot assume that they all agree with the voice from Traveller groups

Carrier testing- it's a no brainer right?

- Genetic testing needs consent
- Dor yeshorim-works for the Jewish population
- Carrier testing has resulted in stigmatisation of carrier women (Sickle cell, Aborigini)
- In Turkey, men invited to get tested on marriage first…
- If we start it amongst Travellers- it has to be on their terms so we don't disadvantage those that test positive?

- Let's adapt carrier testing to our culture?… invite the women..

Rotunda antenatal carrier testing for Galactosemia 01/12/24-31/05/2026

- First carrier testing project amongst Irish Travellers
- Why Galactosemia?- 1/484 -/11 carrier freq
- All Traveller babies fed soy based products until day one Beutler test determines Gal status –policy dates 1980's
- - human rights issue..stigmatisation on ward
- 2% breast feeding rate- could it be improved?**
- Not an invasive test in pregnancy study
- Test the women

Do you want a test to determine whether you can feed your baby whatever way you want when your baby delivers?

Is it going well? Yes!-no coercion

- 55 notified to mid-wife, Approx 80 expected over year
- 25 women (2 man) tested, 2 carriers –hence partners contacted
- 4 cases delivered early, 22 did not take part, 4 consent
- 1 couple high risk, baby expediated testing-positive GAS txed promptly
- 24 women –low risk- can feed their babies whichever way they want
- What about the people who test positive?- how do we capture their feedback?

Lots of planning meetings, form design etc
National roll out- whole diff ball game

Communicating with marginalised groups?

- Most literate
- WhatsApp voice messaging best
- Won’t respond to calls (?Spam)
- QR codes also used
- Younger generation-
- “The times they are a changing?” Bob Dylan

- [Team Aishling Phelan, Cathy Darcy & Valerie O’Leary]
- Catherine Clabby, Trudi McDevitt, Lyndsey Kavanagh & Geraldine McDonnell, Debby Lambert, Fiona Hanrahan, Karen Flood Mike Boyle

Conclusion

- Minimal improvement in health care-30 years
- We don’t know incidence or prevalence of inherited genetic disorders
- Carrier testing-early results pilot Rotunda study promising- 45% take up rate
- Patience-lesson learnt

Time for questions and discussion

- Time for questions

- Satisfaction Survey :

https://forms.office.com/e/DkVu1mktTe

- Website :
  - https://ern-ithaca.eu
  - https://ern-ithaca.eu/webinars/

Thank you for your participation