#### BIOPATH Webinar, 26.10.2022

## Mental Health of Refugee Children: New Findings on Syrian Refugees in Lebanon (BIOPATH Study)









European Commission Horizon 2020 European Union funding for Research & Innovation

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|     | Programn      | ne   |
|-----|---------------|--|
|     | 14·00 – 14 10 | Welcome and Introduction to the  |
|     | 14.00 14.10   | Webinar and BIOPATH: Prof Michael Pluess (QMUL)  |
|     | 14:10 - 14:22 | Prevalence, comorbidity, and predictors of<br>common mental disorders: Dr Fiona McEwen & Dr<br>Claudinei Biazoli (QMUL)                  |
|     | 14:22 – 14:34 | <b>Predictors of psychological risk and resilience</b><br><b>among Syrian refugee children:</b> Ms Cassandra<br>Popham (QMUL)            |
|     | 14:34 - 14:46 | War Exposure, Post-Traumatic Stress Symptoms<br>and Hair Cortisol Concentrations in Syrian Refugee<br>Children: Dr Demelza Smeeth (QMUL) |
|     | 14:46 - 14:52 | Discussion: Prof Elie Karam (IDRAAC)   |
|     | 14:52 - 15:00 | <b>Q&amp;A, Final Comments and End:</b> Prof Michael Pluess (QMUL)   |
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### Background

### Syrian Civil War

- Armed conflict which began in 2011 related to political unrest of the Arab spring across the Middle East
- Initially conflict between Syrian government and rebel groups, developed into complex proxy war
- Detrimental consequences:
  - ➢ Approx. 500,000 casualties
  - 6.7 million Syrians displaced internally within Syria
  - 6.6 million Syrians displayed externally
  - Most remain in the Middle East
  - About 50% of Syrian refugees are children
  - At risk of becoming ill, abused, exploited, no access to school



# Biological Pathways of Risk and Resilience in Syrian Refugee Children Based in Lebanon (вторатн)





Eunice Kennedy Shriver National Institute of Child Health and Human Development

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### **BIOPATH Study**

- Millions of children are affected by war and displacement
  - Some develop psychological problems
  - Some show remarkable resilience
- We investigate the biological underpinnings of individual differences in response to war and displacement

#### Multiple settings

Family, school, community, neighbourhood, services

#### Multilevel approach

Environmental, social, psychological, neuroendocrine, epigenetic and genetic factors

- Focus on both risk and protective factors as well as adaptive and maladaptive outcomes
- Longitudinal design



#### Sample

- N = 1,600 Syrian refugee children (age 8-16 years) and their primary caregiver (Oct 2017 Jan 2018)
  - > 1,009 were followed-up (Oct 2018 Jan 2019)

### **BIOPATH Study**

#### Measures

- Range of questionnaires for child and caregiver
  - Psychopathology outcomes
  - Well-being outcomes
  - Individual, social and environmental protective factors
    - □ Across the various developmental contexts
  - > Individual, social and environmental risk factors
    - □ Across the various developmental contexts
- Biological samples

#### Saliva for molecular variables

Genome-wide genetic information (for GWAS approaches)
 Genome-wide epigenetic information (DNA methylation)

#### > Hair for neuroendocrine variables

- Cortisol
- DHEA-S
- Testosterone



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DE-S-

Male

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Nicolas Chehade, 05/12/2017

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### **Publications**

#### BIOPATH publications related to this webinar

- McEwen, F. S., Popham, C., Moghames, P., Smeeth, D., de Villiers, B., Saab, D., Karam, G., Fayyad, J., Karam, E., & Pluess, M. (2022, Apr). Cohort profile: biological pathways of risk and resilience in Syrian refugee children (BIOPATH). Social Psychiatry and Psychiatric Epidemiology, 57(4), 873-883. https://doi.org/10.1007/s00127-022-02228-8
- McEwen, F. S., Biazoli, C., Popham, C., Moghames, P., Saab, D., Fayyad, J., Bosqui, T., Karam, E., & Pluess, M. (2022). Prevalence and Predictors of Mental Health Problems in Refugee Children Living in Humanitarian Settings. Available at SSRN 4047879.
- Popham, C. M., McEwen, F. S., Karam, E., Fayyad, J., Karam, G., Saab, D., Moghames, P., & Pluess, M. (2022). Predictors of psychological risk and resilience among Syrian refugee children. Journal of Child Psychology and Psychiatry. https://doi.org/10.1111/jcpp.13670
- Smeeth, D., McEwen, F., Popham, C., Karam, E., Fayyad, J., Saab, D., Rieder, M. J., Elzagallaai, A. A., van Uum, S., & Pluess, M. (In Press). War Exposure, Post-Traumatic Stress Symptoms and Hair Cortisol Concentrations in Syrian Refugee Children. Molecular Psychiatry.



# Prevalence, comorbidity, and predictors of mental disorders in refugee children

Dr Fiona McEwen & Dr Claudinei Biazoli

Cassandra M. Popham, Patricia Moghames, Dahlia Saab, John Fayyad, Elie Karam, Tania Bosqui, Michael Pluess

#### **Outline**

Previous evidence

New and improved estimates of common mental disorders in Syrian refugee children living in Lebanon Comorbidity between common mental disorders

Multilevel predictors for symptom burden



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# Previous evidence and gaps in refugee children mental health epidemiology

2 meta-analyses of prevalence & 1 of predictors \*

PTSD: 22.7-52.0%

Anxiety: 15.8–32.0%

Depression: 13.8–28.0%

#### Externalising behaviour problems:

- ODD: 1.7%
- ADHD: 8.6%

**Risk factors**: exposure to trauma, daily stressors, family separation, parent mental health, low SES, bullying, etc.

#### Gaps:

Most data from HIC, lacking data from camps and informal settlements in LMIC

Large variability in estimates between studies

Cross-sectional designs and non-probabilistic sampling

Transcultural measurement errors

Reliance on screening tools with limited data from clinical interviews

\* Henkelmann et al. (2020), BJPsych Open, 6: e68; Blackmore et al. (2020), JAACAP, 59:6; Scharpf et al. (2021), Clin. Psych. Rev, 83



# Estimating prevalence of common mental disorders in the BIOPATH cohort

Settlement-based probabilistic sampling

Longitudinal data

- Culturally adapted structured clinical interviews
  - MINI Kid 6.0
  - Diagnoses agreed by consensus after clinical supervision
  - Contextual, cultural, and linguistic factors that might impact the diagnostic process were taken into account
  - Clinical Global Impression–severity score (CGI-s) ≥ 4 for case definition

Locally validated screening tools for mental health problems



Informal tented settlement in Bekaa, Lebanon



Interview as part of the BIOPATH study © Nour Tayeh, Médecins du Monde France, Lebanon 18/10/2017



#### **Measures**

#### Children's mental health symptoms

Depression: CES-DC, abridged (self-report)

Anxiety: SCARED, abridged (self-report)

PTSD:CPSS (self-report)

Externalising behaviour problems: SDQ + CD/ODD items (caregiver-report)

#### **Risk factors**

**War events**: WEQ (combined self- and caregiver-report)

**Daily stressors**: PREI, developed for BIOPATH (caregiver report)

Child maltreatment: ICAST, abridged (self-report)

**Caregiver-child conflict**: Parent-Adolescent Conflict scale (self-report)

**Caregiver mental health**: PTSD, PCL-5; anxiety, DASS-21; depression, CES-D 10; Impulsiveness, ABIS



#### **Point prevalence estimation**

Cohort-specific cut-offs on screening tools

ROC curve analysis to estimate optimal cut-off for cohort – compares screening tools to clinical interview (reference standard)

Calculate rate of false positives and false negatives when using screening tool

Adjusted prevalence for rate of false positives and false negatives:

Adj. prevalence = (raw prevalence \* PPV) + (1 - raw prevalence \* (1 - NPV))

PPV = Positive predictive value NPV = Negative predictive value



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#### Prevalence – clinical interviews (N=134)

PTSD: 39.6 [31.3–47.9]
Anxiety: 47.8 [39.3–56.3]
Depression: 20.1 [13.3–26.9]
Externalising: 26.9 [19.4–34.4]



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#### **Prevalence – whole sample**

|               | Basel | ine (N=1594)       | Follow | v-up (N=1001)      |
|---------------|-------|--------------------|--------|--------------------|
|               | Raw   | Adjusted           | Raw    | Adjusted           |
| PTSD          | 55.8  | 36.1 [33.7 - 38.5] | 34.7   | 30.4 [27.5 - 33.3] |
| Anxiety       | 78.5  | 54·3 [51·9 - 56·7] | 68.8   | 50·8 [47·7 - 53·9] |
| Depression    | 38.6  | 19·0 [17·1 - 20·9] | 27.2   | 16·1 [13·8 - 18·4] |
| Externalizing | 42.7  | 27·6 [25·4 - 29·8] | 41.6   | 27·2 [24·4 - 30·0] |
| Any CMD       | 92.1  | 58·7 [56·3 - 61·1] | 85.6   | 55·1 [52·0 - 58·2] |



#### Comorbidity

Frequency of overlapping diagnoses

Assigned by clinical interview

Odds ratios calculated to evaluate association between each pair of overlapping disorders





Linear mixed-effects models (LMMs) adjusted for subjects clustered by settlement

Outcomes: total scores for each symptom scale (PTSD, depression, anxiety, externalising)

Covariates: child and caregiver age, child gender, time since leaving Syria as predictors

Sensitivity analyses: only cases with follow-up data; only cases with complete data; in subgroups defined by gender, age, and time since leaving Syria



#### **Predictors**

|                          | Depre       | ession          | Anx         | iety            | PT                 | SD              | Extern      | alizing         |
|--------------------------|-------------|-----------------|-------------|-----------------|--------------------|-----------------|-------------|-----------------|
| Predictor                | Effect Size | <i>p</i> -Value | Effect Size | <i>p-</i> Value | Effect Size        | <i>p</i> -Value | Effect Size | <i>p-</i> Value |
| Time (Follow up)         | - 263       | <∙001           | - 287       | <∙001           | 387                | <∙001           | 079         | ·011            |
| Demographic              |             |                 |             |                 |                    |                 |             |                 |
| Age                      | ·083        | <∙001           | 019         | ·032            | ·061               | <∙001           | -`052       | <∙001           |
| Gender (Female)          | ·099        | ·018            | ·371        | <∙001           | ·058               | ·154            | - 415       | <∙001           |
| Time since leaving Syria | 027         | ·022            | 019         | ·113            | 033                | ·003            | ·034        | ·005            |
| War events               | ·033        | <∙001           | ·022        | < <b>·001</b>   | ·044               | <∙001           | ·023        | < <b>·001</b>   |
| Perceived environment    | - 208       | <∙001           | 070         | ·082            | - <sup>.</sup> 198 | <.001           | -`282       | <∙001           |



#### **Predictors**

|                    | Depre       | ssion           | Anx         | iety            | PT          | SD              | Extern      | alizing         |
|--------------------|-------------|-----------------|-------------|-----------------|-------------|-----------------|-------------|-----------------|
| Predictor          | Effect Size | <i>p</i> -Value | Effect Size | <i>p-</i> Value | Effect Size | <i>p</i> -Value | Effect Size | <i>p</i> -Value |
| Maltreatment       | ·024        | <∙001           | ·018        | <∙001           | ·030        | <∙001           | ·010        | <·001           |
| Conflict           | ·030        | <∙001           | ·007        | ·236            | ·044        | <·001           | ·025        | <∙001           |
| Caregiver symptoms |             |                 |             |                 |             |                 |             |                 |
| Depression         | ·031        | <∙001           | ·019        | <∙001           | ·024        | <∙001           | ·045        | <·001           |
| Anxiety            | ·036        | <∙001           | ·017        | <·001           | ·022        | <·001           | ·041        | <∙001           |
| PTSD               | ·013        | <·001           | ·006        | <·001           | ·007        | <·001           | ·015        | <·001           |
| Impulsivity        | ·023        | <∙001           | ·013        | <∙001           | ·019        | <∙001           | ·034        | <∙001           |



#### **Summary and implications**

The burden of common mental health problems in refugee children is high

Comorbidity is common, providing support for transdiagnostic approaches

- See also Kyrillos et al. (2022), Transcultural Psychiatry

The relative importance of the quality of the environment (daily stressors) highlights the significance of addressing social determinants of mental health

Integrating mental health with other services (e.g. schools) is important

Ultimately policy change aimed at reducing social inequities will be essential



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#### **Acknowledgements**

Michael Pluess, Claudinei Biazoli, Cassandra Popham, Demelza Smeeth, Bernadette de Villiers (*Queen Mary University of London, UK*)

Patricia Moghames, Nicolas Chehade, Vanessa Kyrillos, Stephanie Saad, Diana Abdul Rahman (*Médecins du Monde France, Lebanon*)

Tania Bosqui (American University of Beirut, Lebanon; Trinity College Dublin, Ireland)

Elie Karam<sup>1,2,3</sup>, John Fayyad<sup>1,2,3</sup>, Georges Karam<sup>1,2,3</sup>, Dahlia Saab<sup>1</sup> (<sup>1</sup>IDRAAC, Lebanon; <sup>2</sup>St George Hospital University Medical Center, Lebanon; <sup>3</sup>Balamand University, Lebanon)

And all other members of the BIOPATH team: <u>https://www.qmul.ac.uk/sbbs/about-us/our-departments/psychology/global-mental-health/meet-the-team/</u>

We warmly thank all participating families for their participation

This paper is dedicated to John Fayyad, who sadly passed away during the study





Research for health in humanitarian crises elrha



# Thank you





# Risk and Resilience among Syrian Refugee Children in Lebanon

Cassandra M. Popham, Fiona S. McEwen, Elie Karam, John Fayyad, Georges Karam, Dahlia Saab, Patricia Moghames, Michael Pluess

https://acamh.onlinelibrary\_wiley\_com/doi/10.1111/jcpp.13670





Eunice Kennedy Shriver National Institute of Child Health and Human Development

#### BACKGROUND

- Syrian refugee children are at increased risk of mental health problems
- But some show no evidence of problems, i.e., appear to be resilient
- Many potential predictors (e.g., optimism, coping strategies, parent-child relationship, caregiver mental health, etc)
- But
  - Multiple outcome dimensions
  - Effects of war exposure

RQs: How many children are resilient? What differentiates them from children exposed to the same war events but doing poorly?



#### METHODS

- 1. Operationalise resilience: create low/high symptom groups
- Match each low symptom child with a high symptom child with similar war exposure, age, gender, time since leaving Syria
- 3. Predictors of group membership



#### SAMPLE

- Wave 1 BIOPATH sample
- Exclusions:
  - No reported war exposure (*n* = 49)
  - Missing demographic/symptom data
- 1,528 child-caregiver pairs (590 matched children)
- Mean age = 11.48 (SD = 2.43)
- 52.6% children female
- 89.5% caregivers mother
- M = 9.90 war events (SD = 5.34)
  - 84% witnessed explosions
  - 36.6% witnessed torture
  - 44.4% person close to them killed



#### MANIFESTED RESILIENCE

Evidence of functioning better than expected in the context of adversity

295 (19.3%) children met low symptom criteria



Depression

PTSD

Externalising

#### MATCHED GROUPS

#### War Exposure Item

- 1 Did you witness explosions close to you
- 2 Were you not able to go outside the house because of bullets or bombardment
- 3 Were houses of people you know destroyed
- 3a Did you witness it
- 4 Did your house get completely destroyed or part of it
- 4a Did you witness it
- 5 Were you inside your house when it got bombarded
- 6 Did you witness the kidnapping of someone
- 7 Did any member of your family get kidnapped
- 7a Did you witness it
- 8 Did armed persons try to kidnap you
- 9 Did you witness someone getting beaten up
- 10 Did armed people enter your house
- 10a Did you witness it
- 11 Did you witness persons getting tortured
- 12 Did you get beaten to give information about your parents
- 13 Did you see an injured person (not on TV)
- 14 Did you see armed persons shooting people
- 15 Were you injured from explosions or bombarding
- 16 Was any close person to you injured in war
- 16a Did you witness it
- 17 Did you see a dead person (not on TV)
- 18 Did you witness armed people killing someone
- 19 Did a close person to you get killed
- 19a Did you witness it



#### RESULTS

| Factors                        | OR (95% CI)       | High Symptom (n = 295) | Low Symptom (n = 295)                  |
|--------------------------------|-------------------|------------------------|--|
| individual traits and health   |                   |                        |  |
| Self-esteem                    | 1.51 (1.25, 1.81) |                        |  |
| Optimism                       | 1.07 (1.01, 1.13) |                        | •                                      |
| Support-seeking coping         | 0.93 (0.88, 0.99) |                        |  |
| Problem-focused coping         | 0.91 (0.85, 0.97) |                        |  |
| Avoidance coping               | 0.90 (0.85, 0.96) |                        |  |
| Child general health           | 0.71 (0.58, 0.87) |                        |  |
| Environmental sensitivity      | 0.69 (0.59, 0.82) |                        |  |
| Parent-child relationship      |                   |                        |  |
| Child maltreatment             | 0.96 (0.94, 0.97) |                        |  |
| Maternal psychological control | 0.86 (0.80, 0.93) |                        |  |
| Social environment             |                   |                        |  |
| Perceived social support       | 1.23 (1.02, 1.49) |                        |  |
| Caregiver PTSD                 | 0.98 (0.97, 0.99) |                        |  |
| Bullying                       | 0.96 (0.93, 0.98) |                        |  |
| Caregiver depression           | 0.94 (0.92, 0.97) | •                      |  |
| Caregiver anxiety              | 0.94 (0.91, 0.97) |                        | Significance                           |
| oneliness/social isolation     | 0.85 (0.80, 0.90) | -                      | Combined model     Survived correction |
| Caregiver general health       | 0.81 (0.68, 0.95) |                        |  |
|                                |                   | 0.5 1                  | 0 1.5 2.                               |
|                                |                   | Odd                    | Is Ratios (95% CI)                     |

#### 

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### **INTERPLAY** BETWEEN PREDICTORS

| 1. Optimism   | 6 S <b>1</b> |
|---|--------------|
| 2. Self-efficacy  |              |
| 3. Self-esteem  |              |
| 4. Religiosity  | - 0.8        |
| 5. Future aspirations   | 102020       |
| 6. Future expectations and an |              |
| 7. Future planning  |              |
| 8. Environmental sensitivity  | - 0.6        |
| 9. Problem-focused coping   |              |
| 10. Positive cognitive restructuring  |              |
| 11. Distraction coping  | 0.4          |
| 12. Avoidance coping  | 0.4          |
| 13. Support seeking   |              |
| 14. Maternal acceptance   |              |
| 15. Parental presence   | - 0.2        |
| 16. Parental monitoring   |              |
| 17. Perceived social support  |              |
| 18. Maternal psychological control  |              |
| 19. Parent-child detentment   | 0            |
| 20. Child mainteament   |              |
| 22. Longlings (costal isolation   |              |
| 22. Eureninessisodial isolation   | -0.2         |
| 24. Caregiver any lety  |              |
| 25 Caregiver PTSD   |              |
| 26 Human insecurity at the  |              |
| 27 Perceived refugee environment  | 0.4          |
| 28 Collective efficacy  |              |
| 29. School  |              |
| 30. Parent abroad   | .06          |
| 31. Child responsibilities  | 0.0          |
| 32. Parent deceased   |              |
| 33. Household size  |              |
| 34. Family income   | -0.8         |
| 35. Caregiver employed  |              |
| 36. Household adult literacy  |              |
| 37. Child general health  | 1.           |





#### TO SUMMARISE...

- 19.3% children meet low symptom/resilient criteria
  - But number may be higher
- Several factors predict group membership
  - Parent-child relationship and caregiver mental health important
  - Individual factors (e.g., self-esteem, environmental sensitivity) also important
  - Coping strategies opposite effect than expected
- Correlations between predictors indicate importance of looking at whole context



### THANK YOU!

And credit to: Michael Pluess Fiona McEwen Elie Karam John Fayyad Dahlia Saab Patricia Moghames Demelza Smeeth Claudinei Biazoli Candace Black Child and Youth Development Lab IDRAAC NIH Fieldwork partners & our participants

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# War Exposure, Post-Traumatic Stress Symptoms and Hair Cortisol in Syrian Refugee Children

In Press, Molecular Psychiatry

**Demelza Smeeth**<sup>1</sup>, Cassandra Popham<sup>1</sup>, Fiona S. McEwen<sup>1</sup>, Elie Karam<sup>2</sup>, John Fayyad<sup>2</sup>, Dahlia Saab<sup>2</sup>, Patricia Moghames<sup>2</sup>, Michael J. Rieder<sup>3</sup>, Abdelbaset Elzagallaai<sup>3</sup>, Stan van Uum<sup>3</sup>, Michael Pluess<sup>1</sup>

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3 Northwestern University, Canada

# Cortisol, adversity & mental health

- Adverse events (e.g. war exposure) increases risk of poor mental health
- HPA axis dysregulation a common feature of adversity and/or poor mental health
  - Elevated cortisol, lowered cortisol, altered reactivity, altered trajectories over time
  - Dependent on study design
  - Initial hypersecretion reverts to longer-term hyposecretion
  - Potential as an biomarker of war exposure and PTSD
    - Mixed evidence from adults and adolescents
- Gaps in current literature:
  - Few studies looking at cortisol as a biomarker of war exposure or PTSD in children
  - Few studies on individuals still in adverse environments
  - Studies are often small



Jones, C, Gwenin, C. (2020) Physiological Reports

### **Research questions**

- 1. Is hair cortisol (as a measure of basal cortisol secretion) associated with war exposure?
- 2. Is hair cortisol associated with PTSD symptoms in war-exposed children and adolescents?
- 3. Does hair cortisol mediate the relationship between war exposure and PTSD symptoms?

## Project outline & methodology



Final sample: Y1: n=1579, Y2: n= 933

Adapted from Van Manen, M., et al. PLoS ONE (2019)

# Q1: Is hair cortisol associated with war exposure?

# Hair cortisol is associated with war exposure score



Linear mixed model specification:  $log_{10}cortisol \sim war + batch + (1|participant) + covariates$ 

| Model | Covariates | B (SE) | % Change | р |
|-------|------------|--------|----------|---|
|       |            |        |          |   |

# Age at time of war exposure impacts response to war exposure



Linear mixed model specification:  $log_{10}$  cortisol ~ war + batch + (1|participant) + sex + age at interview

# Hair cortisol decreases with time since leaving Syria





Linear mixed model specification:  $log_{10}$  cortisol ~ war + batch + (1|participant) + sex + age

# Q2: Is hair cortisol associated with PTSD symptoms?

# Hair cortisol is associated with PTSD symptoms



Linear mixed model specification: log10cortisol ~ war + batch + (1|participant) + covariates

|--|

# Q3: Does hair cortisol mediate the relationship between war exposure and PTSD symptoms?

# War exposure, PTSD symptoms and hair cortisol



Both potential mediation models exhibit partial mediation

### **Conclusions & future directions**

- Hair cortisol is weakly associated with war exposure but is confounded by age
  - Future work to disentangle age from war exposure
- Early adolescence may be a particularly sensitive time period
  - Planned replication needed

.

- Hair cortisol is also weakly associated with PTSD symptoms
- > Partial mediation relationships between war exposure, PTSD symptoms and hair cortisol
  - Future work to identify temporal/causal relationships
- Demographic and technical variables more strongly associated with hair cortisol
  - 39.3% increase in HCC from min to max war exposure, 62.7% higher HCC in females

### Thank you for listening

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**Acknowledgments:** QMUL Michael Pluess Fiona McEwen **Cassandra** Popham Claudinei Biazoli **IDRAAQ** Elie Karam John Fayyad Dahlia Saab **Patricia Moghames** Northwestern Michael J. Rieder Abdelbaset Elzagallaai Stan van Uum Thu Chau Meaghan Stolk

NIH Fieldwork partners & our participants









**BIOPATH** webinar

26 October 2022

# Discussion

#### Elie Karam<sup>1-3</sup>, Josleen Barathie<sup>1</sup>

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<sup>3</sup> Department of Psychiatry and Clinical Psychology, St George Hospital University Medical Center, Beirut, Lebanon.

# The uniqueness of the Biopath Study

- Wars (and similar massive catastrophes) are occasions to investigate the effects of trauma on a large scale on humans.
- We were able to watch individual responses to war in refugees and crucially gather the enormous volume of data **prospectively** in an effort to appreciate the intricate nature of environmental, biological and unique personal journeys of each child and adolescent

# **Clinical Applications**

It is obvious that we are finding that the Biopath Study has huge implications in the clinical fields:

- Who gets affected and what happens on follow up ?
- What are the biological reflections of trauma?
- What might be the long-term sequelea of trauma ?
- What factors affect the response to trauma beyond the trauma itself ?

### **Lessons learned so far**

- This is a serious enterprise and a very thrilling scientific journey which has required meticulous attention to a myriad of details not the least being official clearance, local powers, etc...
- Humans look like they are the same everywhere and similar applications abound being in diagnosis or in prediction
- Getting people to engage in treatment is a major challenge in large refugee populations
- The environment where war refugees settle is at least as important as the war trauma they were subjected to.

# Thank you!



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