Training course on causal inference methods and longitudinal modelling in the context of life course trajectory analyses

LifeCycle report D7.5

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List of abbreviations

ATHLETE: Advancing Tools for Human Early Lifecourse Exposome Research and Translation
DOHaD: Developmental Origins of Health and Disease
MR: Mendelian Randomization
WP: work package

Executive summary

Task 7.5 aimed at organizing workshops and courses on causal inference methods and longitudinal modelling in the context of life course research open to researcher within and outside the LifeCycle community. The specific topics for the workshops and courses were identified and discussed during the LifeCycle meetings and the telephone conferences of the work package 7. The following workshops were organized: (i) Hot topics in developmental epidemiology (Rotterdam 2017); (ii) Analytical methods for modelling growth and developmental trajectories (Barcelona, 2018); (iii) Mendelian randomization (Bristol 2019); (iv) Mediation analysis (Online 2020); (v) Statistical analysis to study exposome-health outcome associations: theory and practice (Online 2021); (vi) Transporting estimates across populations: why, when, how (Online 2021); (vii) Conducting mixed effect/trajectory analysis using DataSHIELD (Online 2021); Mediation analysis using DataSHIELD (March 2022). They were closely integrated with the work done for the Lifecycle tutorials and educational papers, and the preparation of the LifeCycle e-learning modules. They involved presenters from different institutions and were open to researchers outside LifeCycle, involving in total more than 400 participants.

1. Introduction

WP7 of LifeCycle focuses on specific methodological aspects of importance for the EU Child Cohort Network and life course research in general. It aims at developing an integrated analysis strategy to apply causal inference methods, model longitudinal data and health trajectories; assessing approaches to analyse multiple exposure data in the context of longitudinal modelling; and enhancing, inside and outside LifeCycle, the knowledge and use of causal inference approaches and methods to model longitudinal data.

Task 7.5 aims at organizing workshops on causal inference methods and longitudinal modelling in the context of life course research, open to researchers within and outside the LifeCycle community. Tasks 7.5 is also informed by the work done under Task 7.1 and Task 7.2 that developed the analysis strategy for LifeCycle (see deliverables 7.1 and 7.2), and by the tutorials prepared under Task 7.4 (see deliverable 7.4).

2. Identification of the specific topics

To answer the main demands for theoretical and applied knowledge emerging from the LifeCycle project, the specific topics for the workshops were identified and discussed during the WP7 sessions at the LifeCycle meetings and the WP7 telephone conferences, and through the work carried out for the five Lifecycle tutorials (see deliverable 7.4).

The following six workshops and one webinar have been organized: (i) Hot topics in developmental epidemiology, Rotterdam, October 2017; (ii) Analytical methods for modelling growth and developmental trajectories, Barcelona, October 2018; (iii) Mendelian randomization, Bristol, November 2019; (iv) Mediation analysis, online October 2020; (v) Statistical analysis to study exposome-health outcome association: theory and practice, online January 2021; (vi) Transporting estimates across populations: why, when, how, online, May 2021; and (vii) Conducting mixed effect/trajectory analysis using DataSHIELD, online October 2021. A seventh workshop on Mediation analysis using DataSHIELD was organized in conjunction with the General Assembly meeting in March 2022. Several LifeCycle partners contributed as presenters and/or scientific organizers. All workshops were open also to researchers external to LifeCycle.

3. Workshops

3.1 Hot topics in developmental epidemiology

This workshop was organized in conjunction with the 10th DOHaD World Congress of the DOHaD Society and the first meeting of the LifeCycle General Assembly on October 15th 2017. It aimed at providing insights into current state of the art methods that allow optimal use of the longitudinal data collected in observational studies. The lectures were given by researchers from the Erasmus MC Rotterdam, the University of Turin and the University of Bristol with the programme detailed in **Table 1.**

Table 1. Programme of the Workshop "Hot topics in developmental epidemiology"

Timetable	Programme
9.00-9.45	**Lorenzo Richiardi (*UNITO*)** Basic of life-course epidemiology studies
9.45-10.30	**Kate Tilling (*UNIVBRIS*)** Longitudinal modelling approaches
10.30-11.00	**Coffee**
11.00-11.45	**Deborah Lawlor (*UNIVBRIS*)** Loss to follow up and selection bias
11.45-12.30	**Nicholas John Timpson (*UNIVBRIS*)** Causal inference methods
12.30-13.30	**Lunch**
13.30-14.15	**Deborah Lawlor (*UNIVBRIS*)** Mediation analysis
14.15-15.00	**Lorenzo Richiardi (*UNITO*)** Confounder selection
15.00-15.30	**Coffee**
15.30-16.15	**Susana Moreira da Silva Santos (ErasmusMC)** Individual participant data meta-analysis
16.15-17.00	**General discussion**

The workshop involved 96 participants. The material was shared with the participants. The workshop contributed to the preparation of a LifeCycle methods article (1), and the LifeCycle e-learning module "Epidemiology: the importance of the study design and confounding" (see deliverable 11.4).

3.2 Analytical methods for modelling growth and developmental trajectories

This workshop was organized in conjunction with the second meeting of the LifeCycle General Assembly on October 24th 2018. It aimed at providing insights into the approaches to model repeat measurements with focus on multilevel models, knitting together trajectories from multiple studies, and longitudinal modelling with DataSHIELD. The lectures were given by researchers from the University of Bristol and the University College London according with the programme detailed in **Table 2**.

Table 2. Programme of the Workshop "Analytical methods for modelling growth and developmental trajectories"

Timetable	Programme
8.15-8.30	**Coffee**
8.45-8.45	**Lorenzo Richiardi (*UNITO*), Martine Vrijheid (*ISGlobal*)** Welcome and objectives
8.45-9.45	**Deborah Lawlor (*UNIVBRIS*)** Intro to modelling repeated data and methods when applied to a single study
9.45-10.45	**Laura Howe (*UNIVBRIS*), Deborah Lawlor (*UNIVBRIS*)** Multilevel models: practical tips
10.45-11.15	**Coffee**
11.15-12.15	**Rachael Hughes (*UNIVBRIS*)** Lifecourse trajectory across numerous cohorts
12.15-13.00	**Elinor Jones (*University College London*)** Analysis of data that cannot be pooled: current capability in DataSHIELD and future directions
13.00-13.30	**General discussion**
13.30-14.30	**Lunch**

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The workshop involved 60 participants. The material was shared with the participants. The workshop contributed to the preparation of two LifeCycle methods articles (2,3).

3.3 Mendelian randomization

This workshop was organized in conjunction with the third meeting of the LifeCycle General Assembly on November 29th 2019. It aimed at providing insights into different Mendelian Randomization methodologies with applications to real data using the R software. The lectures were given by researchers from the University of Bristol with the programme detailed in **Table 3**.

Table 3. Programme of the Workshop "Mendelian randomization"

Timetable	Programme
8.45-9.00	**Registration**
9.00-9.45	**Eleonor Sanderson (*UNIVBRIS*)** One sample mendelian randomization (MR)
9.45-10.30	**Eleonor Sanderson (*UNIVBRIS*)** One sample MR analysis demonstration
10.30-10.45	**Coffee**
10.45-11.30	**Deborah Lawlor (*UNIVBRIS*)** Introduction to two sample MR
11.30-12.30	**George Davey Smith (*UNIVBRIS*)** Latest updates in MR
12.30-13.30	**Lunch**
13.30-14.30	**Caroline Borges (*UNIVBRIS*)** Two sample MR
14.30-16.00	**Kaitlin Wade (*UNIVBRIS*)** MR-base platform introduction & demonstration (optional)
16.00-16.30	**Deborah Lawlor (*UNIVBRIS*)** Q&A and extended discussion (optional)

The workshop involved 36 participants. The material was shared with the participants.

3.4 Mediation analysis

This workshop was organized in conjunction with the fourth meeting of the LifeCycle General Assembly on October 19th 2020, and was held remotely due to the Covid-19 pandemic. It aimed at providing insights into the statistical approaches to mediation analysis with applications to real data using the R software. The lectures were given by researchers from the University of Turin with the programme detailed in **Table 4**.

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Table 4. Programme of the Workshop "Mediation analysis"

Timetable	Programme
11.30-13.00	**Lorenzo Richiardi (*UNITO*)** Introduction to mediation analysis Potential outcomes Controlled and natural effects and their identification Decompositions
13.00-14.00	Lunch
14.00-16.00	**Daniela Zugna (*UNITO*)** Statistical approaches to mediation analysis Application using R & discussion

The workshop was followed by 90 participants and was video recorded. The material was shared with the participants and videos are publicly available online through the LifeCycle Youtube channel (https://www.youtube.com/channel/UCrenSIv4N-unFsVuPR_xqZA/videos). The workshop contributed to the preparation of a LifeCycle methods article (4).

3.5 Statistical analysis to study exposome-health outcome associations: theory and practice

This workshop was developed in the context of the European project ATHLETE and also delivered to LifeCycle members on May 20th 2021. It was held remotely due to the Covid-19 pandemic. This workshop aimed at providing insights into the statistical methods to study exposome-health associations, the data pre-processing steps to perform such analysis and the use of r*exposome* package available in the R software. The lectures were given by a researcher from ISGlobal, Barcelona, with the programme detailed in **Table 5**.

Table 5. Programme of the Workshop "Statistical analysis to study exposome-health outcome associations: theory and practice"

Timetable	Programme
11.00-13.00	**Charline Warembourg (*ISGlobal*)** Statistical challenges and available statistical methods to study exposome-health associations Data pre-processing *rexposome* package Practice with R

The workshop was followed by 55 participants. The material was shared with the participants. The video is publicly available online through the ATHETE Youtube channel (https://www.youtube.com/watch?v=HSLVQqsOsig).

3.6 Transporting estimates across populations: why, when, how

This webinar was organized on May 20th 2021 and was held remotely due to the Covid-19 pandemic. It aimed to introduce the concept of transportability, the underlying assumptions to transport the estimates from a reference population to a target population and the statistical methods available to perform such analysis. The lecture was led by researchers from University of Turin with the programme detailed in **Table 6**.

Table 6. Programme of the Webinar "Transporting estimates across populations: why, when, how"

Timetable	Programme
14.00-14.15	**Lorenzo Richiardi (*UNITO*)** Introduction
14.15-15.30	**Ghislaine Scelo (*UNITO*)** Introduction to transportability through some applied examples

The webinar was followed by 53 participants and was video recorded. The material was shared with the participants, and videos are publicly available online (https://www.youtube.com/watch?v=e3DAAvMFe08). The workshop contributed to the preparation of a LifeCycle methods article (5).

3.7 Conducting mixed effect/trajectory analysis using DataSHIELD

This workshop was organized in conjunction with the fifth meeting of the LifeCycle General Assembly on October 27th 2021 and was held remotely due to the Covid-19 pandemic. It aimed at showing how to perform longitudinal analyses, specifically the mixed effect/multilevel models, in DataSHIELD. The lectures were given by researchers from the University of Bristol with the programme detailed in **Table 7**.

Table 7. Programme of the Workshop "Conducting mixed effect/trajectory analysis using DataSHIELD"

Timetable	Programme
12.15-14.15	**Tim Cadman (*UNIVBRIS)* Brief introduction to mixed effects / multi-level models Practical 1: Visualising data and modelling linear trajectories Practical 2: Modelling non-linear trajectories

The workshop was followed by 40 participants and was video recorded. The material was shared with the participants. Videos and slides are available at and available through the DataShiled website (https://www.datashield.org/help/get-started/specialist-workshops#trajectory-analysis-2021).

3.8 Mediation analysis in DataSHIELD

This workshop was held in Paris in conjunction with the last LifeCycle General Assembly on May 19th 2022. It aimed at showing how to perform mediation analysis in DataSHIELD using the *dsMediation* package, which was finalized thanks to a LifeCycle fellowship. The lectures were given by researchers of the University of Copenhagen and the University of Turin, with the programme detailed in **Table 8**.

Table 8. Programme of the Workshop "Mediation analysis in DataSHIELD"

Timetable	Programme
13.45-15.15	**Demetris Avraam (UCPH) and Daniela Zugna (UNITO)** Brief introduction to mediation analysis Practical: Mediation analysis with binary exposure and mediator/continuous exposure and mediator

The workshop was followed by 29 participants. The material was shared with the participants. The workshop will contribute to an additional LifeCycle tutorial on mediation analysis in DataShield (see deliverable 7.4).

4. Conclusions

We have provided in this report a description of the LifeCycle workshops and training courses organized with the aim of responding to the main needs of the LifeCycle community and consequently to a broader research community. Workshops were organized in conjunction with the Lifecycle General Assembly meetings and were open for the research community outside LifeCycle. The related material was shared with the participants. During the COVID-19 pandemic the workshops were held online, and their videos are publicly available. In total the workshops were attended by more than 400 participants.

5. Contributions of partners

- **UNITO**: led the Task, organized the workshops, gave lectures, handled the material after the workshops
- **UNIVBRIS**: contributed to the organization of the workshops, and gave lectures
- **ISGLOBAL**: gave lectures
- **ERASMUS**: contributed to the organization of the workshop, gave lectures

6. Deviations from the original plan

This deliverable has been fulfilled fully in line with the original plan as stated in the grant agreement. Between 2020 and 2021, due to the COVID-19 pandemic, the workshops were held online and recorded. Their videos are publicly available.

7. Dissemination activities

All workshops were open and advertised to both LifeCycle researchers and researchers outside the project. To facilitate participation they were held in conjunction with the General Assembly meetings. The workshop materials were shared with the participants. Online workshops were also video recorded and their videos are publicly available.

8. References

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4. Zugna D, Popovic M, Fasanelli F, Heude B, Scelo G, Richiardi L. Applied causal inference methods for sequential mediators. Research Square. 2021.
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