Breakout sessions: Physical health: Obesity

Auditorium

15:50-17:10

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Pathways between socioeconomic disadvantage and growth in the Scottish Longitudinal Study, 1991-2001

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Introduction
Background

- Social inequalities in health are well established.

- Early years of development play a critical role in the creation of socioeconomic health inequalities.

- A better understanding of the mediatory pathways through which social disadvantage affects childhood growth might give rise to plausible interventions.

- Childhood height often used as a marker of childhood health and development.

- Childhood obesity associated with adulthood obesity, an established risk factor for diabetes, cardiovascular disease and cancer. Growing childhood obesity epidemic in recent decades.

- Both childhood obesity and height are socially patterned.

- In current study aim to elucidate the mediatory role of birth weight.
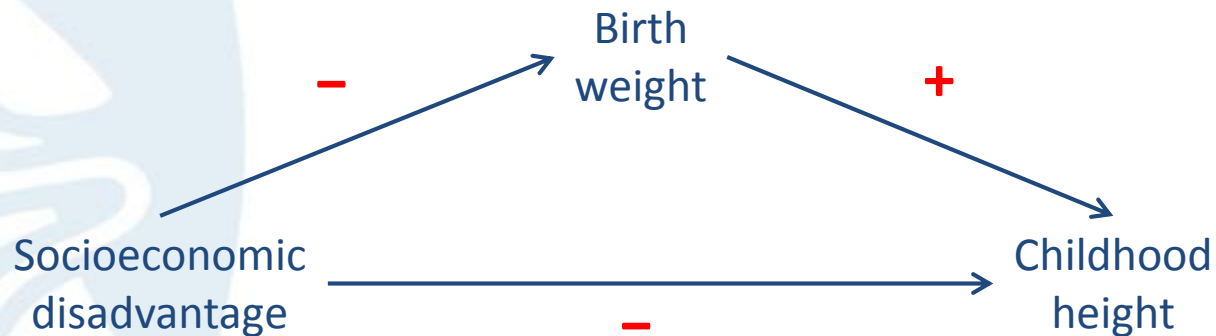
Introduction
Childhood height

- Socioeconomic disadvantage → reduced childhood height.
- Socioeconomic disadvantage → lower birth weight.
- Higher birth weight → increased childhood height.

Introduction
Childhood height

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- Higher birth weight → increased childhood height.
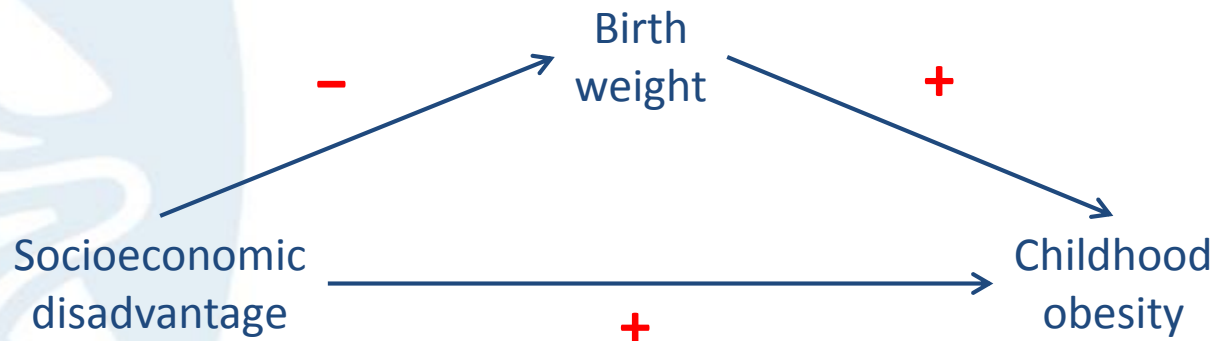
Birth
weight

−

+
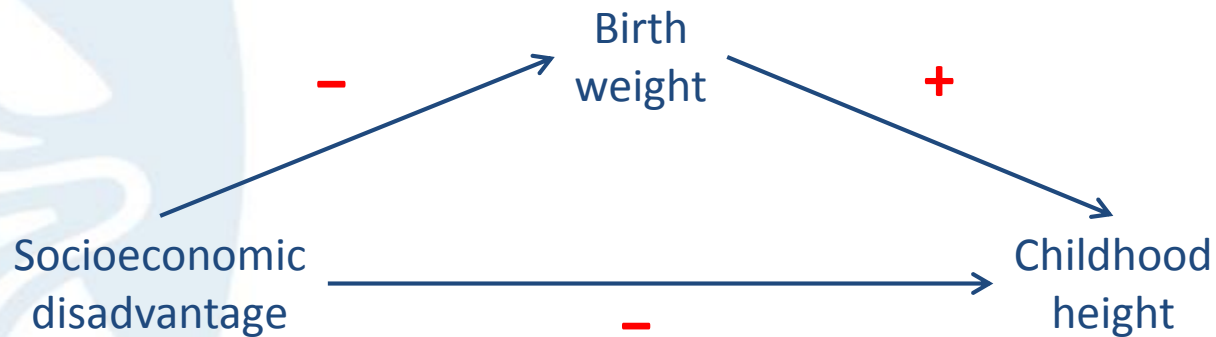
Socioeconomic
disadvantage

Childhood
height

−

- Direct effect: -ve
- Indirect effect: -ve
- 'Consistent mediation'

Introduction
Childhood obesity

- Socioeconomic disadvantage → increased childhood obesity.
- Socioeconomic disadvantage → lower birth weight.
- Higher birth weight → increased childhood obesity.
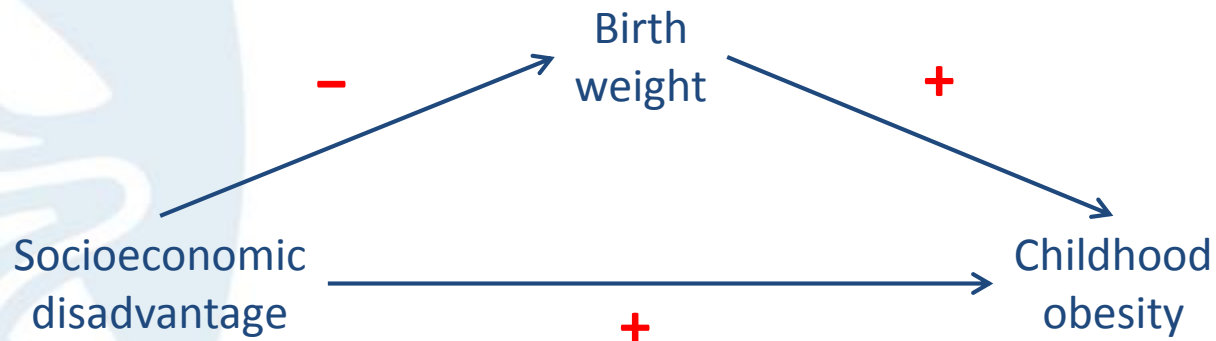
Introduction
Childhood obesity

- Socioeconomic disadvantage → increased childhood obesity.

- Socioeconomic disadvantage → lower birth weight.

- Higher birth weight → increased childhood obesity.

- Direct effect: +ve

- Indirect effect: -ve

- 'Inconsistent mediation'

Methods
Study participants

- Scottish Longitudinal Study (SLS) is a large-scale, anonymised linkage study and is a 5.3% sample of the Scottish population, selected using 20 birth dates.

- The sample considered for the present analysis are the ~43,000 SLS members born from 1991 to 2001.

- Data mainly from Census.

- Linkage to other data sources: birth variables from maternity and birth records; childhood growth data from Pre-School Child Health Systems Programme.

- No identifiable individual level data. Derived from linkages that are anonymised prior to analysis by the research team.

Methods
Socioeconomic disadvantage

Mother's education:

- Derived from 2001 Census data.

- Categorised as: 'no qualifications', 'GCSE or equivalent', 'A-level or equivalent', 'degree or equivalent '.

Scottish Index of Multiple Deprivation (SIMD):

- Multiple deprivation across several domains: current income, employment, health, education skills and training, geographic access to services and housing.

- Derived using the postcode recorded on the birth record.

- Analysed in quarters of the observed distribution.

Methods
Socioeconomic disadvantage

Synthetic weekly income:

- Clemens & Dibben (2014) proposed a method to derive a synthetic measure of weekly wage using observed data on occupation.

- Multilevel model of wage predicted by Standard Occupational Classification in the UK Labour Force Survey (2001–2010) (plus age and sex). Externally validated and tested.

- Applied in SLS to mother's and father's reported occupation at birth of child.

- Analysed as quarters of the observed distribution.

Methods

Anthropometric data

- Height, weight and age at ages 6-8 weeks, 8-9 weeks, 21-24 months, 39-42 months and 48 months.

- Growth models used to define the outcomes: height and (binary) overweight at age 4.5 years.
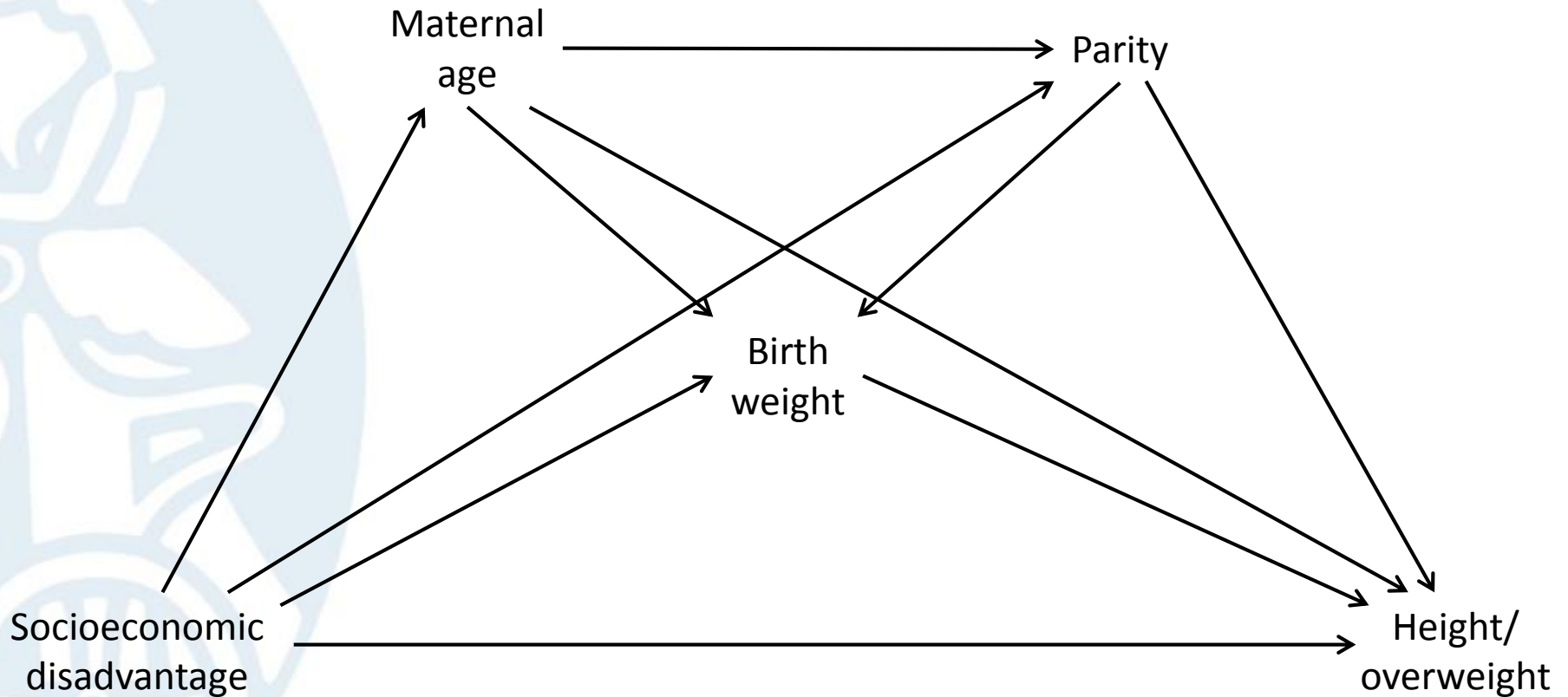
Potential mediator

- Birth weight (<2.50 kg, 2.50-2.99 kg, 3.00-3.49 kg, 3.50+ kg).

Potential confounders

- Sex, year of birth (1991-1994, 1995-1998, 1999-2001), Health Board (10 regions), ethnic group (white, non-white), maternal age (<20, 20-24, 25-29, 30-34, 35+), parity (0, 1, 2+).

Methods
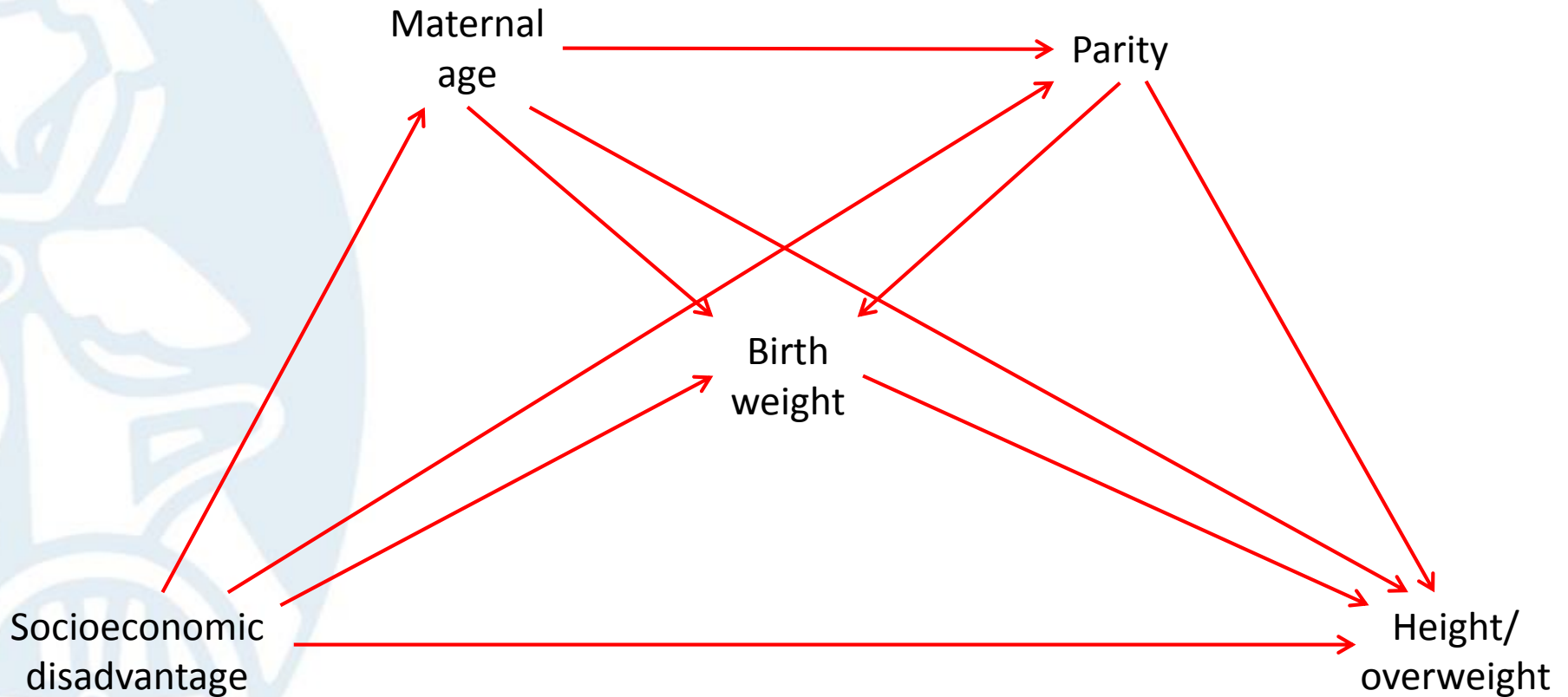## Causal diagram

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.

Methods
Total effect

Maternal age

Parity

Birth weight

Socioeconomic disadvantage

Height/ overweight

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.

Methods

Direct effect not via birth weight
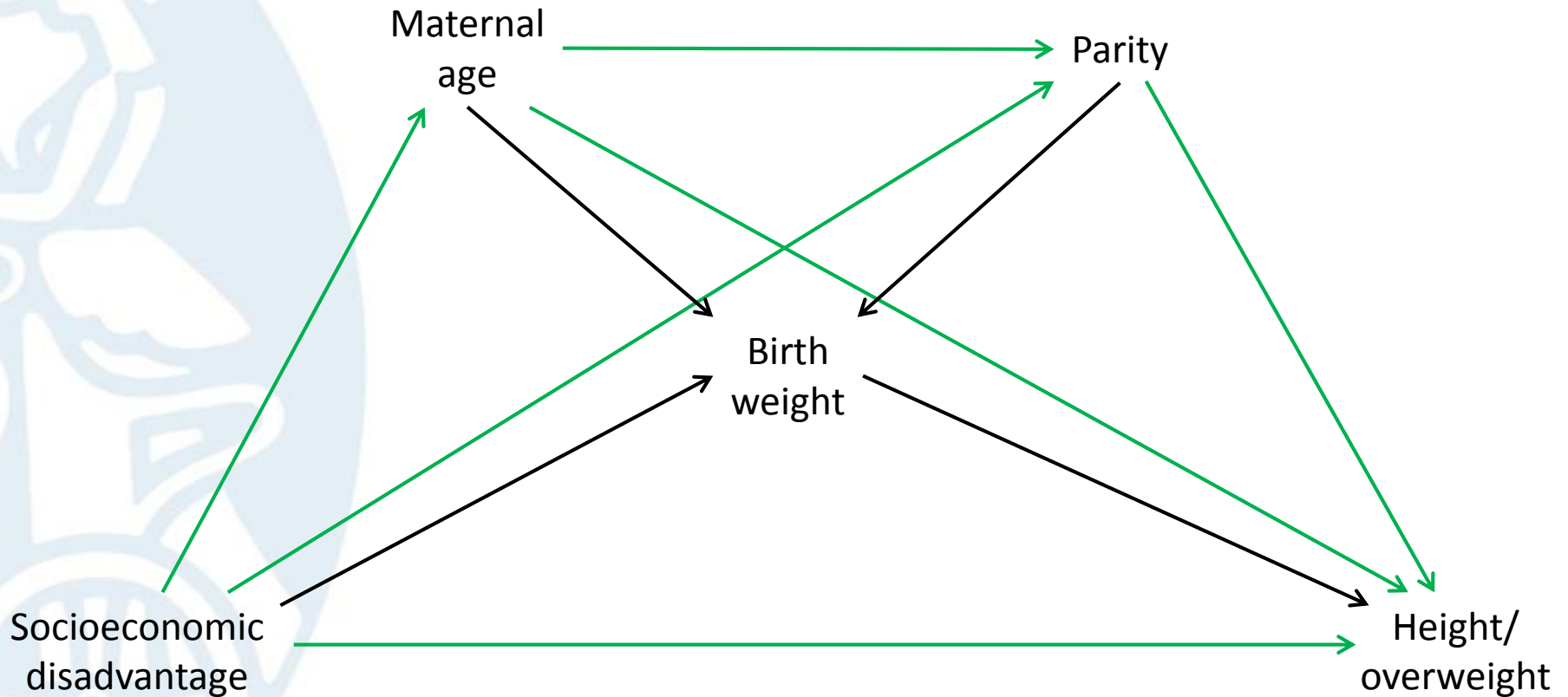

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.

Methods

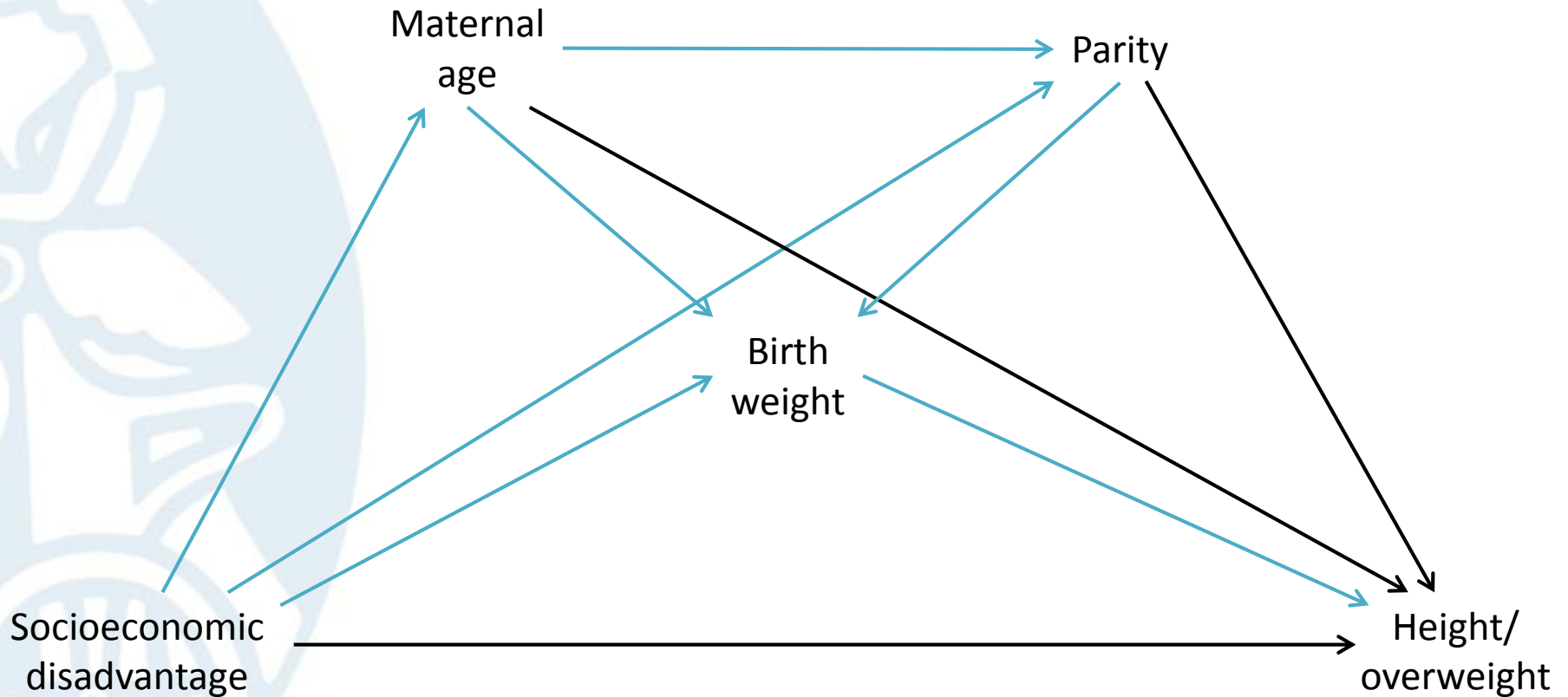## Indirect effect via birth weight

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.

Methods
Traditional mediation analysis

- Height and overweight at age 4.5 years related to indicators of socioeconomic disadvantage using linear and logistic regression. Fit two models:

    (A) Confounder adjusted (sex, year of birth, Health Board and ethnicity);

    (B) Additionally adjusted for birth weight.

- Regression coefficient for socioeconomic disadvantage in Model (A) gives 'total effect', in Model (B) gives 'direct effect'.

- Analyses restricted to complete cases only.

- Height analyses weighted by the inverse of the approximate variance of predicted height. Overweight analyses weighted by the inverse of the product of the approximate variances of predicted height and weight.

- Robust SE estimator.

Methods
Traditional mediation analysis

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.
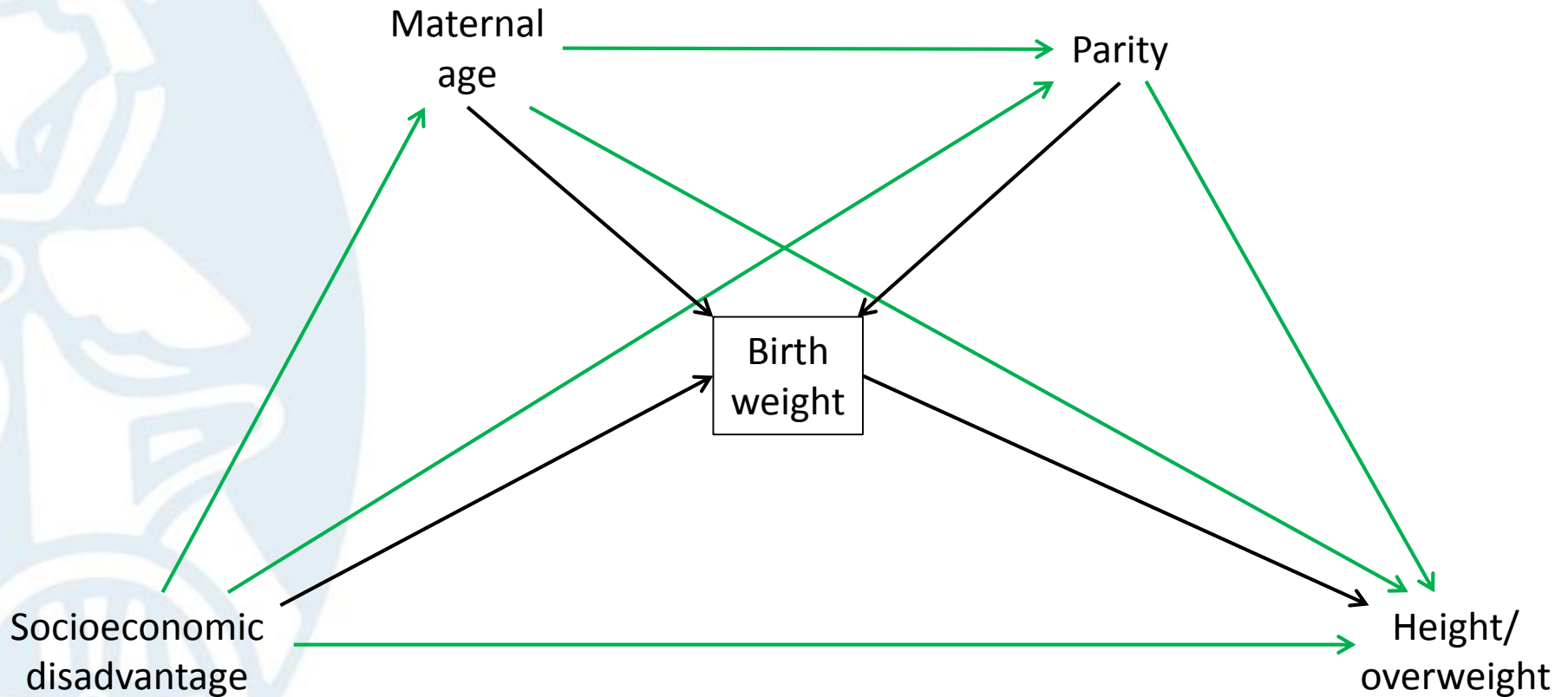
Methods
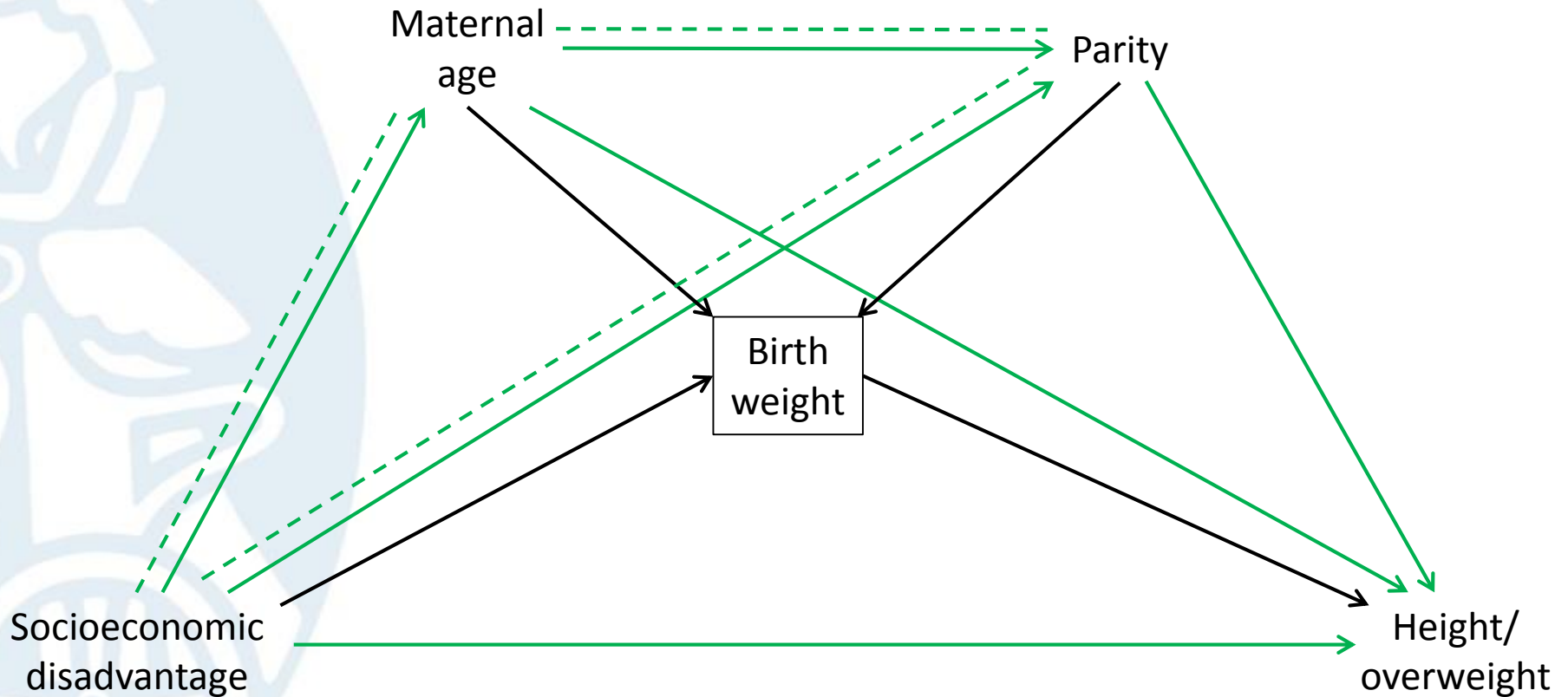## Traditional mediation analysis

Background confounders (sex, year of birth, Health Board and ethnicity) allowed to affect all variables in the diagram.

Methods
Counterfactual-based mediation analysis

- *Total causal effect* of socioeconomic disadvantage on height/weight at age 4.5 years decomposed into *natural direct effect* (not via birth weight) and *natural indirect effect* (via birth weight).

- Estimation performed via parametric G-computation (Robins [1986]) using Monte Carlo simulation using the gformula package in Stata (Daniel [2011]).

- Outline:
  i.   Model relationships between variables in the observed data;
  ii. Simulate forwards in time under different hypothetical interventions;
  iii. Compare outcomes.

- Maternal age and parity considered as intermediate confounders.

- Complete case analysis to allow comparison.

- SEs obtained using bootstrap.

Results

Height at age 4.5 years (cm) - traditional mediation analysis

	Confounder adjusted				Additionally adjusted for birth weight			
	Coeff	95% CI	p overall (p trend)		Coeff	95% CI	p overall (p trend)	Proportion mediated
Mother's education (n = 15,031)								
No qualifications	-0.98	-1.22, -0.75	<0.001		-0.56	-0.79, -0.33	<0.001	0.43
GCSE or equivalent	-0.50	-0.69, -0.32			-0.28	-0.46, -0.10		0.44
A-level of equivalent	0.02	-0.17, 0.22			0.11	-0.08, 0.30		-
Degree or equivalent	0.00	(ref)			0.00	(ref)		
SIMD quarter (n = 16,588)								
1 (most deprived)	-0.91	-1.10, -0.72	<0.001		-0.55	-0.73, -0.36	<0.001	0.40
2	-0.44	-0.62, -0.25	(<0.001)		-0.27	-0.45, -0.09	(<0.001)	0.39
3	-0.25	-0.44, -0.06			-0.19	-0.37, 0.00		0.24
4 (least deprived)	0.00	(ref)			0.00	(ref)		
Synthetic income quarter (n = 16,627)								
1 (lowest)	-0.75	-0.97, -0.54	<0.001		-0.09	-0.32, 0.13	0.001	0.88
2	-0.59	-0.80, -0.38			-0.14	-0.35, 0.07		0.76
3	-0.04	-0.24, 0.17			0.20	0.01, 0.40		-
4 (highest)	0.00	(ref)			0.00	(ref)		

Results

Height at age 4.5 years (cm) – counterfactual-based mediation analysis

	Total causal effect				Natural direct effect			Proportion mediated
	Coeff	**95% CI**	**p**		**Coeff**	**95% CI**	**p**	
Mother's education (n = 15,031)								
No qualifications	-0.97	-1.19, -0.75	<0.001		-0.77	-0.99, -0.56	<0.001	0.20
GCSE or equivalent	-0.47	-0.64, -0.29	<0.001		-0.32	-0.50, -0.15	<0.001	0.30
A-level of equivalent	0.01	-0.17, 0.19	0.92		0.09	-0.09, 0.27	0.32	-
Degree or equivalent	0.00	(ref)			0.00	(ref)		
SIMD quarter (n = 16,588)								
1 (most deprived)	-0.92	-1.09, -0.75	<0.001		-0.74	-0.91, -0.56	<0.001	0.20
2	-0.43	-0.61, -0.26	<0.001		-0.33	-0.50, -0.16	<0.001	0.24
3	-0.26	-0.43, -0.09	0.003		-0.18	-0.35, -0.02	0.03	0.28
4 (least deprived)	0.00	(ref)			0.00	(ref)		
Synthetic income quarter (n = 16,627)								
1 (lowest)	-0.69	-0.90, -0.48	<0.001		-0.58	-0.78, -0.37	<0.001	0.16
2	-0.54	-0.74, -0.35	<0.001		-0.44	-0.63, -0.25	<0.001	0.19
3	0.01	-0.18, 0.20	0.91		0.11	-0.07, 0.30	0.23	-
4 (highest)	0.00	(ref)			0.00	(ref)		

Results

Overweight at age 4.5 years - traditional mediation analysis

	Confounder adjusted				Additionally adjusted for birth weight			
	OR	95% CI	p overall (p trend)		OR	95% CI	p overall (p trend)	Proportion mediated
Mother's education (n = 14,935)								
No qualifications	1.26	1.05, 1.52	0.08		1.45	1.20, 1.75	0.001	0.27
GCSE or equivalent	1.15	0.99, 1.34	(0.02)		1.23	1.06, 1.44	(<0.001)	0.25
A-level of equivalent	1.17	1.00, 1.37			1.20	1.03, 1.41		0.12
Degree or equivalent	1.00	(ref)			1.00	(ref)		
SIMD quarter (n = 16,477)								
1 (most deprived)	1.22	1.04, 1.42	0.05		1.35	1.16, 1.58	0.001	0.25
2	1.19	1.02, 1.38	(0.01)		1.24	1.07, 1.44	(<0.001)	0.16
3	1.18	1.01, 1.37			1.20	1.03, 1.40		0.08
4 (least deprived)	1.00	(ref)			1.00	(ref)		
Synthetic income quarter (n = 16,516)								
1 (lowest)	1.09	0.92, 1.29	0.53		1.20	1.00, 1.45	0.12	0.35
2	1.02	0.87, 1.21	(0.25)		1.09	0.92, 1.29	(0.03)	0.44
3	0.97	0.83, 1.14			1.01	0.86, 1.18		-
4 (highest)	1.00	(ref)			1.00	(ref)		

Results

Overweight at age 4.5 years - counterfactual-based mediation analysis

	Total causal effect				Natural direct effect			
	OR	95% CI	p		OR	95% CI	p	Proportion mediated
Mother's education (n = 14,935)								
No qualifications	1.21	1.03, 1.42	0.02		1.28	1.08, 1.50	0.003	0.19
GCSE or equivalent	1.10	0.97, 1.25	0.15		1.15	1.01, 1.31	0.04	0.23
A-level of equivalent	1.16	1.02, 1.33	0.03		1.19	1.04, 1.36	0.01	0.11
Degree or equivalent	1.00	(ref)			1.00	(ref)		
SIMD quarter (n = 16,477)								
1 (most deprived)	1.19	1.03, 1.36	0.01		1.25	1.09, 1.43	0.002	0.18
2	1.13	0.99, 1.29	0.08		1.16	1.01, 1.33	0.03	0.15
3	1.12	0.98, 1.28	0.10		1.14	1.00, 1.31	0.06	0.12
4 (least deprived)	1.00	(ref)			1.00	(ref)		
Synthetic income quarter (n = 16,516)								
1 (lowest)	1.05	0.90, 1.22	0.56		1.08	0.93, 1.26	0.32	0.29
2	1.02	0.88, 1.17	0.83		1.04	0.90, 1.20	0.56	0.38
3	0.98	0.85, 1.13	0.81		1.01	0.88, 1.16	0.90	-
4 (highest)	1.00	(ref)			1.00	(ref)		

Summary
Conclusions

- Strong, graded, negative effect of each measure of socioeconomic disadvantage on height at age 4.5 years, mediated to some extent by birth weight.

- Strong, graded, positive direct effect of each measure of socioeconomic disadvantage (with the exception of synthetic income) on overweight at age 4.5 years, partly masked by inconsistent mediation by birth weight.

- Few previous studies have explicitly looked at this mediation.

- Suggest that interventions to increase birth weight in more disadvantaged groups may reduce social inequalities in height, but also *increase* social inequalities in overweight.

- Extent of mediation overestimated in the traditional mediation analysis due to inappropriate handling of intermediate confounding – essential to appropriately handle intermediate confounding in mediation analyses.

- Cross-study comparisons could assess the generalisability of these substantive findings to other settings.

Summary
Limitations

- Both analyses assume no unmeasured exposure-mediator, exposure-outcome or mediator-outcome confounding.

- Missing data.

- Phased implementation of Pre-School Child Health Systems Programme across Health Boards (mean 1994, range 1991 to 2000).

- Analyses restricted to Scottish-born SLS members.

- Lack of appropriate propagation of uncertainty from growth modelling into mediation analysis.

Acknowledgements

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Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000; 320: 1240-3.

Daniel RM, De Stavola BL, Cousens SN. gformula: Estimating causal effects in the presence of time-varying confounding or mediation using the g-computation formula. The Stata Journal. 2011; 11: 479-517.

Robins J. A new approach to causal inference in mortality studies with a sustained exposure period - application to control of the healthy worker survivor effect. Mathematical Modelling. 1986; 7: 1393–512.

Methods
Growth modelling

- Height and weight modelled separately in males and females using mixed effects Berkey-Reed models (Berkey [1987]):

$$y_{ij} = (\beta_0 + \beta_{0i}) + (\beta_1 + \beta_{1i})x_{ij} + \beta_2 \log(x_{ij}) + \beta_3(1/x_{ij}) + \varepsilon_{ij}$$

- Unstructured variance-covariance matrix.

- Allowed for heteroskedastic residual errors.

- All subjects with at least one measurement included.

- Fitted models used to predict subject-specific fitted height and weight at age 4.5 years.

- Approximate variance of each predicted height and weight value estimated as a function of the estimated variances of the random terms.

- Predicted BMI at age 4.5 years derived using predicted height and weight at age 4.5 years.

- Sex-specific overweight cut-offs (Cole et al [2000]) used to define overweight at age 4.5 years.

Methods
Counterfactual-based mediation analysis

- *Total causal effect*. A comparison of two hypothetical worlds: in the first everybody is exposed and in the second nobody is exposed.

- *Natural direct effect*. A comparison of two hypothetical worlds: in the first everybody is exposed and in the second nobody is exposed; in both worlds, the mediator is set to the value it would naturally take in the absence of exposure.

- *Natural indirect effect*. A comparison of two hypothetical worlds: in the first the mediator is set the value it would take in the presence of exposure and in the second the mediator is set the value it would take in the absence of exposure; in both worlds the exposure is set to be present.

- Total causal effect of socioeconomic disadvantage on height/weight at age 4.5 years decomposed into natural direct effect (not via birth weight) and natural indirect effect (via birth weight).

Closing plenary session
Auditorium

17:10-17:40

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Thank you

Wine reception
17:40 -18:15

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