UNIVERSITY OF LINCOLN

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Analyses of longitudinal health data

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Background

- Panel data (aka longitudinal data, repeated measures) are repeated observations on the same cross-section

	Cups of tea		
Name	**Morning**	**Noon**	**Night**
Murray	*x*	*y*	*z*
Merilyn	*p*	*q*	*r*

	Cups of tea				Dog owner
Name	Week	Morning	Noon	Night	
Murray	*Monday*	*x*	*y*	*z*	*Yes*
Murray	*Next Monday*	*a*	*b*	*c*	*Yes*
Merilyn	*Monday*	*p*	*q*	*r*	*No*
Merilyn	*Next Monday*	*s*	*t*	*u*	*No*

	Cups on Monday			Cups on Monday week			Dog owner
Name	am	noon	pm	am	noon	pm	
Murray	*x*	*y*	*z*	*a*	*b*	*c*	*Yes*
Merilyn	*p*	*q*	*r*	*s*	*t*	*u*	*No*

Panel data $\{Y_{it}\}$

where index $i = 1, \ldots, N$ runs across individuals

and index $t = 1, \ldots, T$ runs across time periods

with potential to have a grand total of up to NT observations recorded on variable Y

Magic and Magic2

- Functional constipation in children is common with pooled prevalence of 14% for ages 0-18 years
- Management is challenging and based on reported symptoms
- An objective measure of whole gut transit time (WGTT) could assist in directing therapy
- Under standard care, measuring WGTT involves using X-ray radiopaque markers. Main drawbacks:
  (i) it provides an ionising radiation dose, and
  (ii) it is unable to accurately define the colon anatomy
- Magnetic resonance imaging (MRI) can offer a better alternative

The mini-capsules (TransiCap®, JEB Technologies Ltd) are classed as an inertmarker ingestible medical device (European Union Class IIa). They enter the body via the oral cavity and travel inside the GI tract where they can be located using MRI

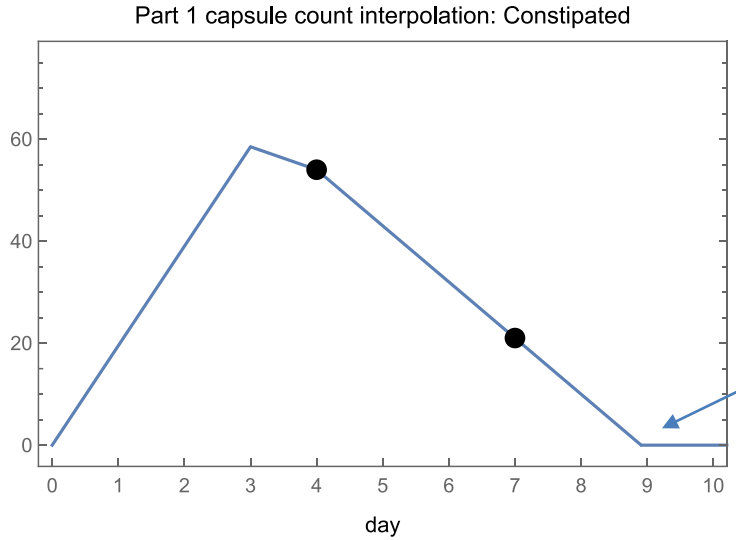
Child swallows 24 capsules per day on 3 consecutive days (day 1, 2, 3)

MRI scans taken on day 4 and day 7

MHRA asked for information:

(i) How long will it take until all capsules are expelled from the body?
(ii) Does ingestion of capsules have an adverse effect on health?

Time to complete expulsion



2-wave panel data with observations on days 4 and 7

Predicted to clear all mini-caps after approx 9 days

Magic data on n=16 constipated; mean predicted clearance 8.3 days

54	44	54	31	53	47	68	52	57	51	55	62	72	70	65	72
21	1	0	0	6	3	68	0	9	14	0	21	72	70	0	25

Magic data on n=19 healthy controls; mean predicted clearance 7.5 days

58	23	38	45	19	25	36	16	43	15	23	19	48	18	38	16	43	46	26
3	0	16	17	10	0	0	3	0	0	0	7	9	0	0	0	3	12	0

Mini-caps and health

$EQVAS_{it}$ = CYP self-rated health on day t
(score between 0 (worst) and 100 (best); baseline is day 0)

$Ingest24_{it}$ = 1 if 24 mini-capsules ingested on day t, 0 otherwise

$Numcaps_{it}$ = piecewise linear interpolation for the number of mini-caps in body on day t

Model the baseline adjusted change in self-reported health using individual fixed effects

$\{EQVAS_{it} - EQVAS_{i0}\}$	**Healthy Controls** (N=15, NT=115)	**Constipated** (N=11, NT=115)
Ingest24	-2.10 (se=1.12; p=0.03)	3.21 (se=1.94; p=0.95)
Numcaps	-0.08 (se=0.05; p=0.04)	-0.10 (se=0.05; p=0.09)

Health adversely affected in the controls but probable placebo effect in the target group

British Lung Foundation

Economic Evaluation of Sport England's Active Steps

- Active Steps is remote health coaching – BLF Helpline, website, social media platforms – designed to engage inactive people living with chronic lung conditions to become and stay physically active over a 12 month period

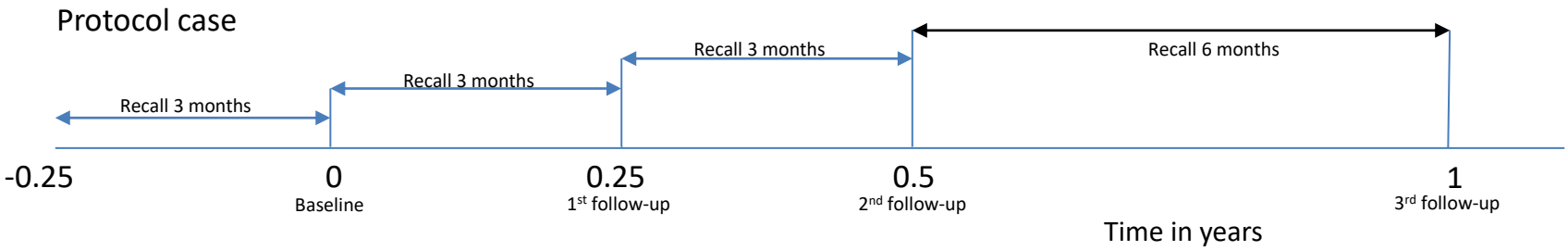
- Independent, parallel standard care trial assigned a similar protocol served as the control arm

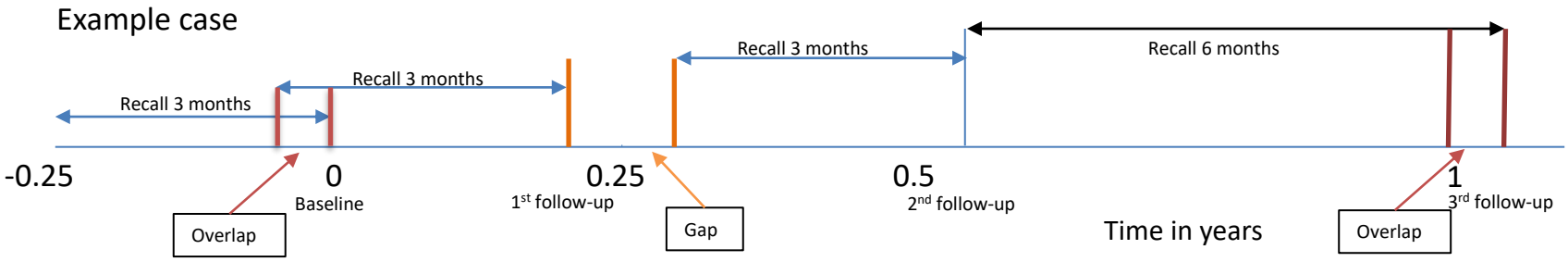
- Data collections scheduled at baseline, 3, 6 and 12 months create a set of panel data

- For the economic evaluation the standard measures were to be gathered:
  - EuroQoL EQ-5D health-related quality of life
  - Bespoke NHS resource use questionnaire with 3-month recall when used at baseline, 3- and 6-month follow-ups and 6-month recall when used at the 12-month follow-up
- Baselines
  - Active Steps: 177 taken between 4 Feb 2019 and 19 Mar 2020
  - Control: 77 taken between 26 Jul 2019 and 27 Dec 2019
- … and then COVID-19 and social distancing and furlough and lockdowns and extreme clinical vulnerabilities and shielding happened

- Economic dropouts – 36% in Active Steps (only 4% in Control)
- 5 known deaths
- Many data follow-ups missing
- Many data follow-ups mistimed
- Summary - an abundance of protocol violations

- Example: Active Steps baseline 4 Feb 2019 (1st recruit)
  - Follow-up 1: scheduled 4 May 2019, conducted 10 May 2019
  - Follow-up 2: scheduled 4 Aug 2019, conducted 12 Aug 2019
  - Follow-up 3: scheduled 4 Feb 2020, conducted 29 Apr 2020 (85 days late)


Protocol case
Recall 3 months
Recall 3 months
Recall 3 months
Recall 6 months
-0.25
0
Baseline
0.25
1st follow-up
0.5
2nd follow-up
1
3rd follow-up
Time in years


Example case
Recall 3 months
Recall 3 months
Recall 3 months
Recall 6 months
-0.25
0
Baseline
0.25
1st follow-up
0.5
2nd follow-up
1
3rd follow-up
Time in years
Overlap
Gap
Overlap

Summary of deterministic economic results: MRC Dyspnoea 3-5 subgroup

	Aggregate cost (£)	Recall years	Total cost (£ pa)	Total QALY	Life years	QALY (QALY pa)	ICER (£/QALY)
MRC Dyspnoea 3-5							
AS (n=63)	67,940	30.1	2,254	20.7	37.8	0.547	
IC (n=51)	84,671	38.5	2,200	20.9	39.9	0.523	2,237
difference			53			0.024	
MRC Dyspnoea 3-5 ignore protocol violations							
AS (n=63)	69,444	31.0	2,240	19.9	36.0	0.552	
IC (n=51)	90,450	36.0	2,141	22.3	42.75	0.522	3,294
difference			99			0.030	

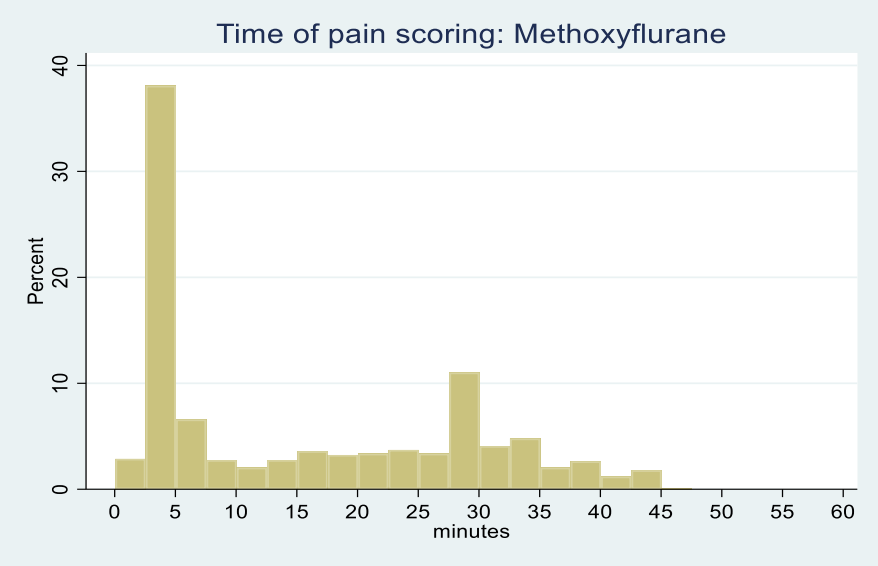
Note: from baselines, the annualised total cost COVID-19 unaffected averages £3,755

Green Whistle

Penthrox® methoxyflurane

- Methoxyflurane (Penthrox®; Galen Ltd) is a volatile fluorinated hydrocarbon anaesthetic with analgesic properties in sub-anaesthetic doses
- European licence for emergency relief of moderate to severe pain in conscious adults with trauma pain
- Limited evidence of benefits and costs in the prehospital setting
- Pain score (0-10) and the time when taken are the two key pieces of data

Pain scores



#Scores	Freq
2	432
3	330 (76.4%)
4	59 (13.7%)
5	10 (2.3%)
6	3 (0.7%)
7	1 (0.2%)

Name	Score 1	Time 1	Score 2	Time 2	Score 3	Time 3	…
PID 001	S_{11}	T_{11}	S_{12}	T_{12}	S_{13}	T_{13}	…
PID 002	S_{21}	T_{21}	S_{22}	T_{22}	S_{23}	T_{23}	…
PID 003	S_{31}	T_{31}	S_{32}	T_{32}	S_{33}	T_{33}	…

Panel data: Pain scores by patient and number taken

$\{S_{ij}\}$ S_{ij} denotes the pain score reported by patient $i = 1, \ldots, N$ taken in sequence $j = 0,1, \ldots, T_i$ over time, where S_{i0} denotes the baseline score and T_i is the total number of scores taken on patient i while under analgesia.

$\{t_{ij}\}$ The time (in minutes) at which the j^{th} pain score is taken on the i^{th} patient is denoted $t_{ij} \geq 0$, where baseline $t_{i0} = 0$.

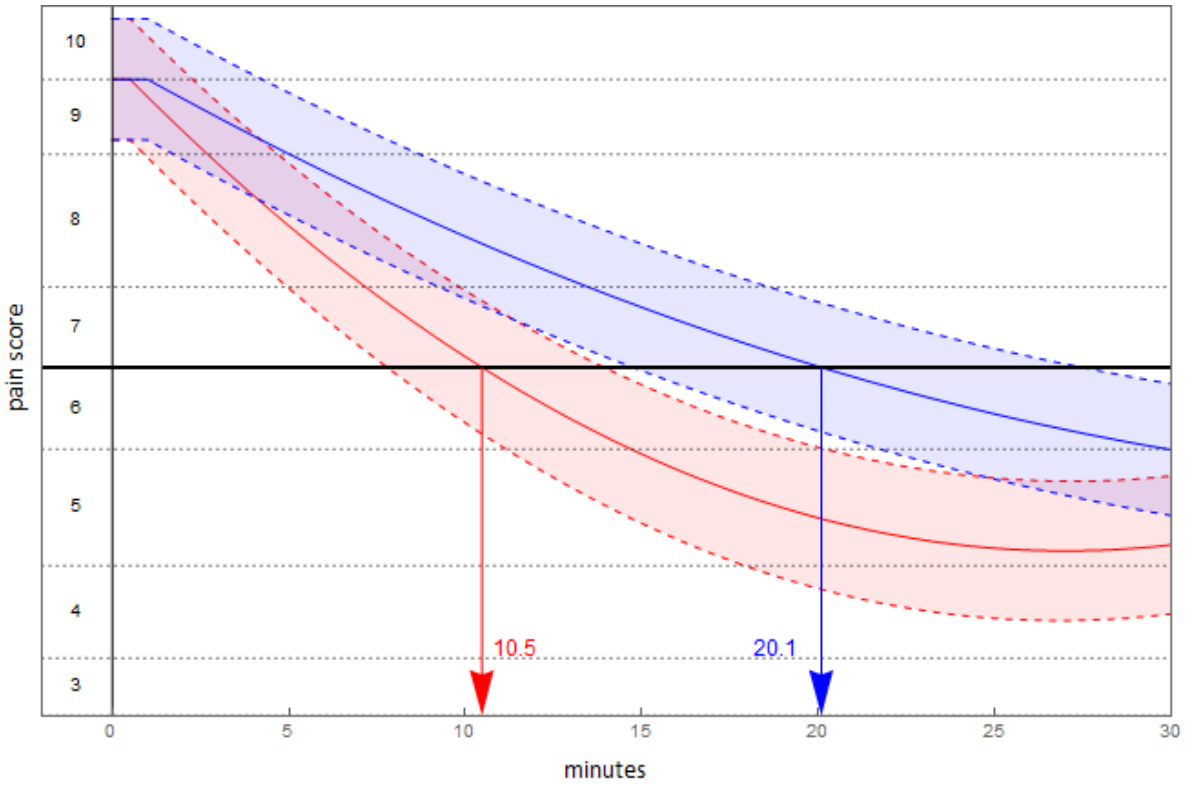
Modelling approach:

$\text{Pain} = f(time)$ diminishing at a decreasing rate under analgesia

$$S_{ij} = \beta_0 + \beta_1 t_{ij} + \beta_2 t_{ij}^2 + \cdots$$ quadratic in time

expect $\beta_1 < 0$ and small $\beta_2 > 0$
speed of effect depends mainly on β_1

Predicted pain pathways: methoxyflurane (red), morphine IV (blue)



Thank you

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