Cerebral palsy: causes, care and compensation costs

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Cerebral Palsy: questions

- What is it?
- How common is it?
- Why does it matter?
- How is it treated?
- How is it prevented?
- What does it cost?

Cerebral Palsy: health and social implications

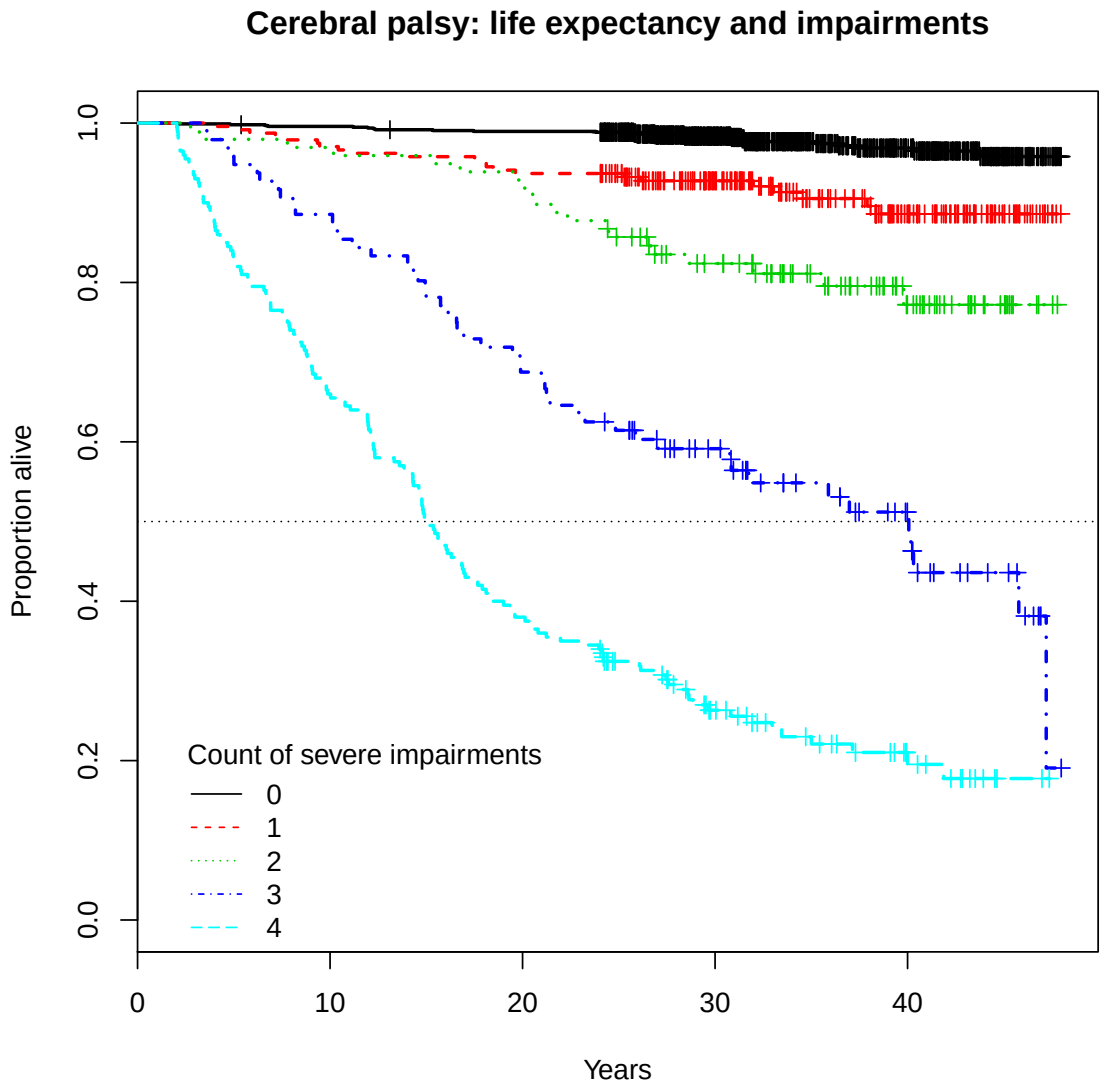
- What is it?
  Disorders of movement and posture attributed to disturbances in developing fetal of infant brain.
- How common is it?
  - 2.0 to 3.5 per 1000 live births (everywhere!)
  - most common cause of physical disability
  - 1560 to 2720 of births in UK per year
- Why does it matter?
  - care needed, depending on impairments:
  - ambulation, manual dexterity, mentabl ability, vision.
- How much care is needed?
  - 61% have no severe impairments
  - 20% have 3 or 4 severe impairments
  - life expectancy varies substantially with severity
  - families provide much of the care

Normal birthweight infants have more severe impairments.

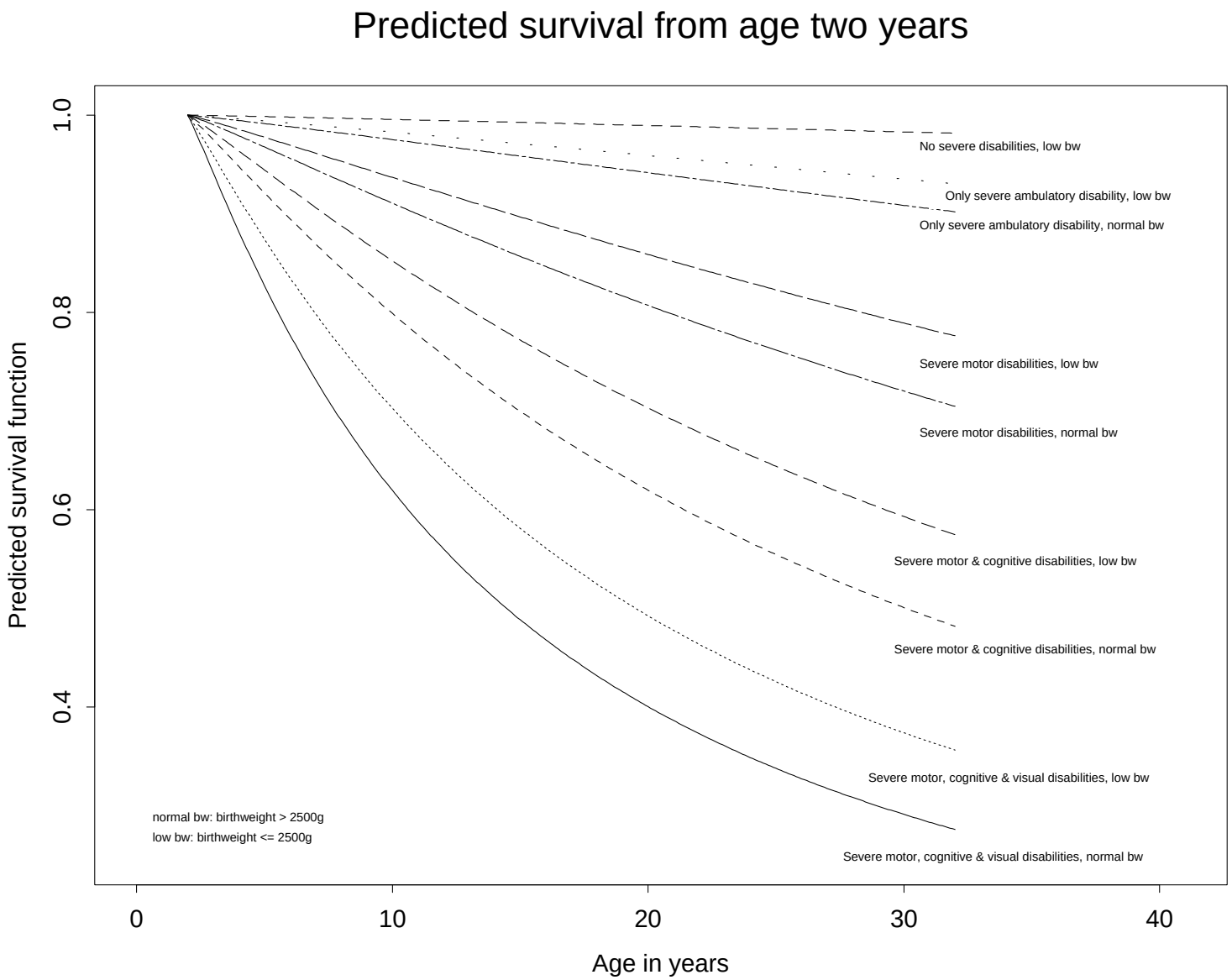
Cerebral Palsy: how many older people?

I wonder if you could help. I'm trying to find out the number of older people with CP (55yrs and over) in Scotland. I realise that such figures are hard to come by. The CP Register for Scotland only have details of those born with CP from 1990 onwards and are not aware of any information on the numbers among older people. It's been suggested the it might be possible to use survival estimates, along with populations sizes for the relevant years of birth.
Thank you
Kevin
Dr. Kevin Paterson
Strathclyde Centre for Disability Research

Cerebral Palsy: how many older people?



Cerebral Palsy: how many older people?



Statistical model

Let **t** denote lifetime, **Amb** indicate whether in wheel-chair, **Mand** indicate able to feed and dress self, **IQ** denote IQ level, **Blind** indicate blindness, **Lowbw** indicate low birth weight ($\leq 2500g$), and **x** a vector of all covariates.

$$log(T_x) = 11.37 - 1.11Amb - 1.02Mand - 0.81IQ - 0.70Blind$$

$$-0.02Lowbw + \epsilon,$$

where ϵ is a random variable with a logistic distribution,

$$S(t) = \frac{x^{-1/0.76}}{1 + x^{-1/0.76}}.$$

Cerebral Palsy: how many older people?

We can fit various statistical models, but models must be checked.
Do we have the right data?

- Estimates up to age 48 years.
- Parents of 48 year old people with cerebral palsy are old!
- Scottish register started in 1990.
- Case series from Bristol with births from 1940.
- Selection of people with CP who saw a particular consultant.
- Missing information on impairments.

We need to model the effect of selection into the study.
We need to assess the impact of missing data: model the propensity of missing covariates, interdependence of lifetime and missingness.
Closed skew normal distributions provide a class of models for selection of participants, loss to follow-up and incomplete data.

Cerebral Palsy: cost of care?

Girl injured at birth awarded £11m in compensation
The £10.8m settlement is believed to be one of the largest in a case of medical negligence. a lump sum of £5.9m and periodic payments throughout her life that will rise to £204,000 a year.

. . . wins £5m from NHS Lanarkshire over brain damage to son

In general, claims of this nature are valued at between £1 million to £7 million.

total of 542 claims for cerebral palsy cost the NHS some £1.3bn
Report from the NHS Litigation Authority, 2000-2010.

Cerebral Palsy: cost of care?

Dear Professor Hutton

John Smith v Royal Coventry Hospital

I act on behalf of John Smith, who was born on 1 May 2003 at Royal Coventry Hospital. My client's claim is being pursued through the High Court. The Defendants have made some admissions in relation to both breach of duty and causation. John suffers from cerebral palsy, with profound developmental delay and quadraplegia. He has severe visual impairment, and suffers from epilepsy. I write to see whether you and Professor Pharoah would be willing to prepare a report on life expectancy in this case.

Cerebral Palsy: cost - treatment, prevention

- What is it?
- How common is it?
- Why does it matter?
- How is it treated?
- How is it prevented?
- What does it cost?

"evidence of benefits of drugs, surgery, therapies is weak"
Colver, Fairhurst, Pharoah (2014), *The Lancet*

Cerebral Palsy: prevention - risk factors

Risk factors: associations, not causes

- Gestational age and birthweight
  - 90 cases per 1000 neonatal survivors birthweight $< 1000g$
  - 1.5 cases per 1000 neonatal survivors birthweight $\geq 2500g$
  - Lower risk with 'right' birthweight for gestational age
- Multiple births:
  - Twins relative risk 5.6
  - Triplets relative risk 12.3
  - Two live born twins: 18 per 1000
  - Same-sex survivor, co-twin infant death: 167 per 1000
  - Vanishing twins
- birth asphyxia
- infections of mother or infant

Cerebral Palsy: clinical negligence?

About 10% might be due to clinical negligence
Mis-managed birth caused birth asphyxia and cerebral palsy?
or
pre-birth brain injury (cerebral palsy) caused difficult birth?
"The most common cause is that the brain is damaged secondary to prematurity. About 40 per cent of children with cerebral palsy are premature." (GOSH)
So - why premature?
Assisted conception might contribute to increase in cerebral palsy through multiple births.
Missing information: assisted conception is confidential in most countries.

Cerebral Palsy: Vanishing twins hypothesis

The twin my baby will never know Telegraph 28 Apr 2014

. . . the (12-week) scan I can clearly see Adriana's tiny, dead twin. . . . completely formed, curled up in its own little sac. Twin two had died at around eight weeks' gestation, I was told.

http://www.telegraph.co.uk/news/health/children/10789160/The-twin-my-baby-will-never-know.html

The dead twin might contribute in various ways to injury of the living twin.

The prevalence of vanishing twins is unknown.

A dead twin seen on a scan might not be mentioned.

Some of the dis-appearance is due to changes in law: a fetus papyraceus in the placenta is no longer recorded.

Cerebral Palsy: Vanishing twins

Testing the hypothesis poses several severe challenges.

- Recruit women to have very early scans to check for twins
- Keep track of the women and their infants
- Screen all the placentas
- Record all still births
- Record all deaths before age 5
- Confirm all diagnoses by age 6

Cerebral palsy might be suspected early in very severely affected infants; diagnosis is generally confirmed about age 5 years. What about deaths before diagnosis?
The Big Data enthusiasts will think of routinely collected data, which will have selected people, selected times of scans, and plenty of missing data. How do we deal with this complexity?

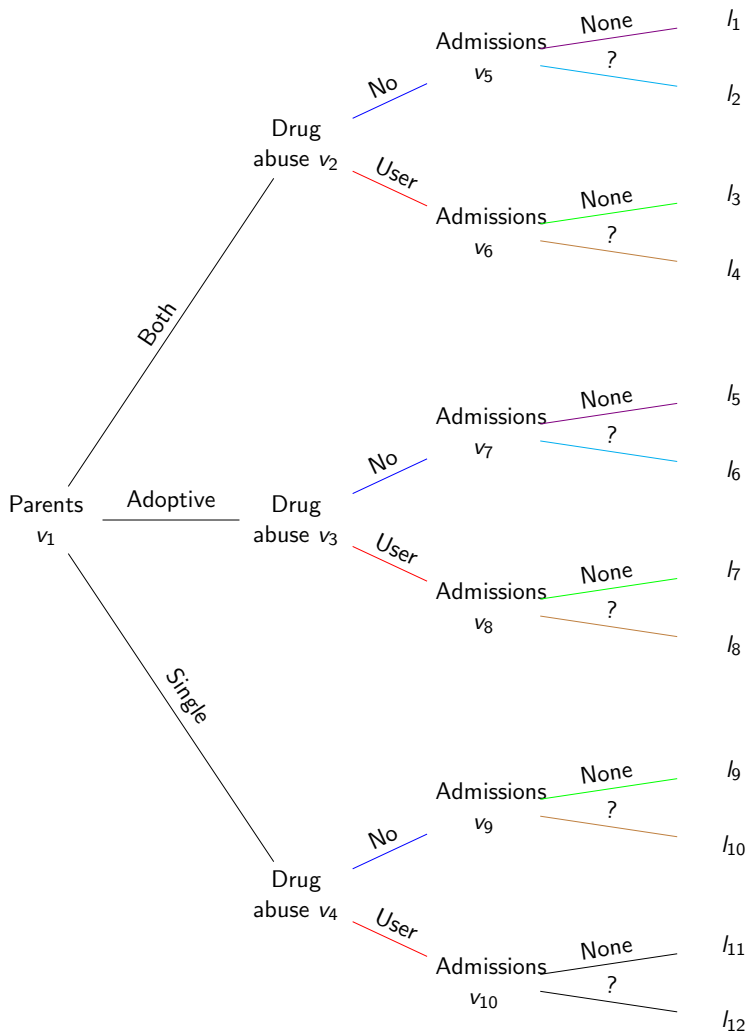
Graphical Models

- Graphical models are statistical models which describe a joint probability function of random variables in terms of a graph
- The graph provides an accessible, visual representation of the statistical model
- Existing graphical models: Gaussian Graphical Models; Log-Linear Models and Bayesian Networks

Chain Event Graphs (Smith and Anderson, 2008)

- Derived from probability trees by merging nodes in tree with the same associated conditional probabilities
- Extended to ordinal chain event graphs to explore missing data (Barclay, Hutton, Smith, 2014)

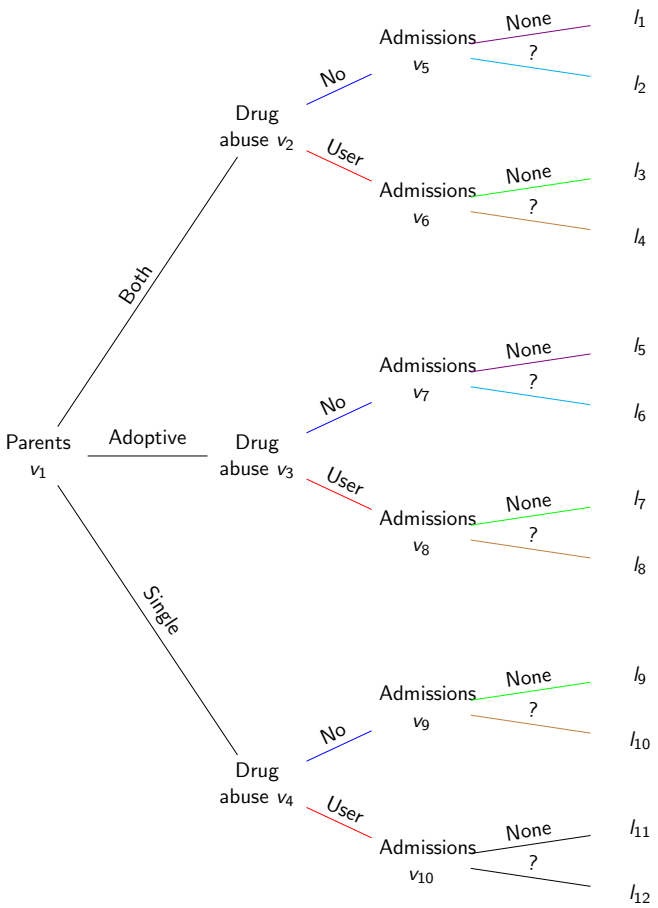
CEG: Initial tree - a longitudinal study example



- Parents:
  - both
  - single
  - adoptive
- Drug abuse age 16-18:
  - no
  - user
  - missing
- Hospital admissions:
  - none
  - some or missing

Lines are same colour if they represent the same conditional probability

CEG: Stages and positions of a tree



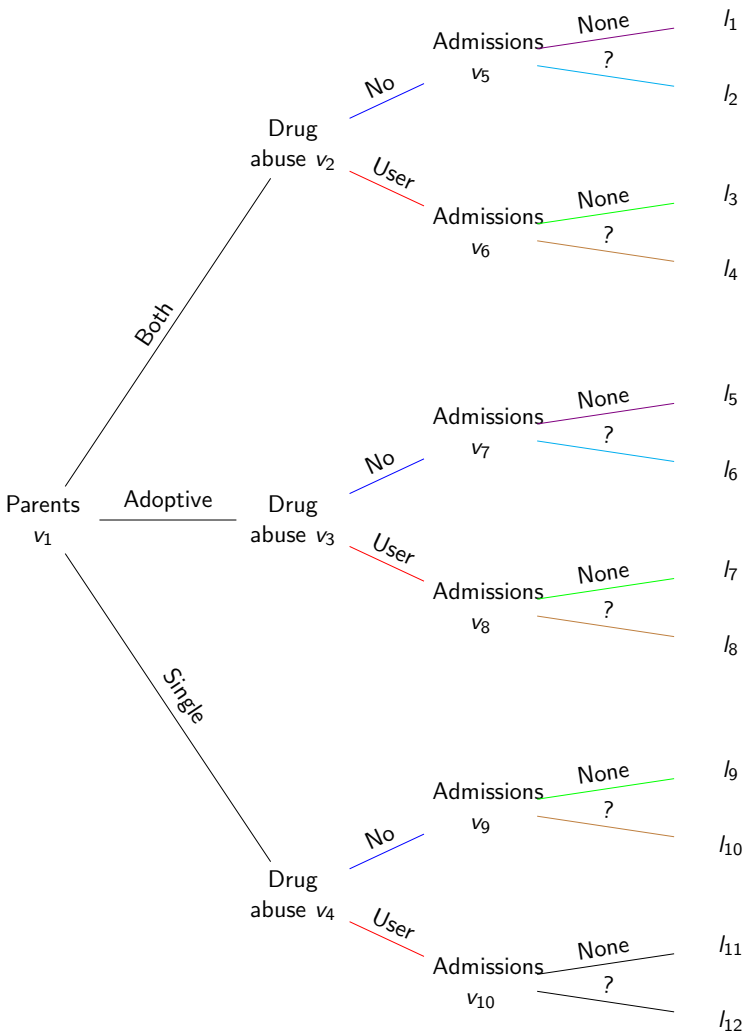
Two situations v, v' are in the same **stage** u if and only if

- The topology of their florets $F(v)$ and $F(v')$ are the same
- There is a bijection between the florets such that the probabilities on corresponding edges are the same

Two situations v, v' are in the same **position** w if and only if

- The topology of their subtrees $T(v)$ and $T(v')$ are the same
- There is a bijection between the subtrees such that the probabilities on corresponding edges are the same

CEG: Stages and Positions



- **Stages:**

$$u_1 = \{v_1\}, u_2 = \{v_2, v_3, v_4\},$$

$$u_3 = \{v_5, v_7\}, u_4 = \{v_6, v_8, v_9\},$$

$$u_5 = \{v_{10}\}$$

- **Positions:**

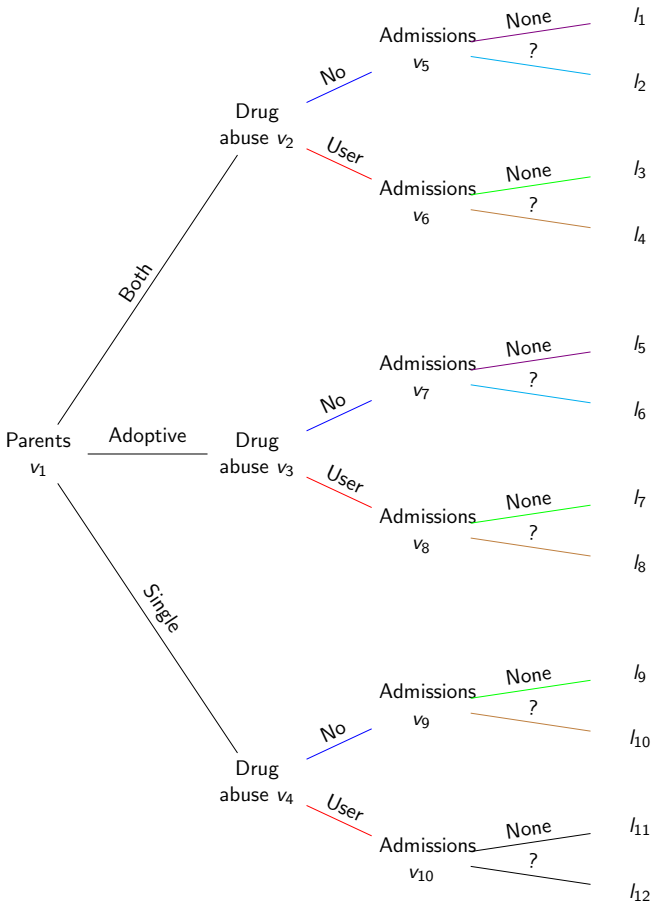
$$w_1 = \{v_1\}, w_2 = \{v_2, v_3\},$$

$$w_3 = \{v_4\}, w_4 = \{v_5, v_7\},$$

$$w_5 = \{v_6, v_8, v_9\}, w_6 = \{v_{10}\}$$

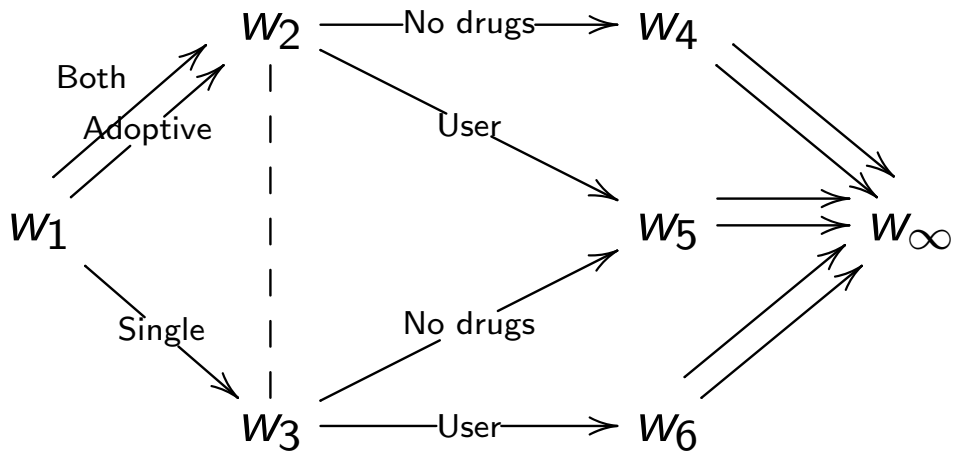
$$w_\infty = \{l_1, l_2, l_3, \ldots, l_{10}, l_{11}, l_{12}\}$$

Definition of a Chain Event Graph



- The set of vertices is the set of all positions of the tree T and the position of all leaf nodes.
- For each position w choose a single representative situation $v(w)$. We have an edge from w to w' for each edge from $v(w)$ to a vertex $v' \in w'$.
- If $u(w) \neq \{w\}$, there is more than one position in the stage, so we connect two positions by an undirected dotted line.

Example of a Chain Event Graph derived from tree



w_1 = Root, w_2 = Both or adoptive parents, w_3 = Single parent,
w_4 = Both or adoptive parents and no drug abuse,
w_5 = (Both or adoptive parents and drug abuse)
or (Single parent and no drug abuse),
w_6 = Single parent and drug abuse, w_∞ = Sink.

Score of the CEG

- Let Π_u be the set of conditional probabilities associated with the floret $F(u)$
- $\Pi_u \sim Dir(\boldsymbol{\alpha}_u)$, $\boldsymbol{\alpha}_u = (\alpha_{u1}, .., \alpha_{ur_u})$
- $\Pi_u | D \sim Dir(\boldsymbol{\alpha}_u + \mathbf{N}_u)$, $\mathbf{N}_u = (N_{u1}, .., N_{ur_u})$
- Simplest case: uniform prior on the root-to-leaf paths of the associated tree

The score of a CEG structure C given a dataset D is $\log L(C|D) =:$

$$\sum_{u \in J(T)} \left(\log \Gamma(\alpha_u) - \log \Gamma(\alpha_u + N_u) + \sum_{k=1}^{r_u} \{ \log \Gamma(\alpha_{uk} + N_{uk}) - \log \Gamma(\alpha_{uk}) \} \right)$$

We compare two CEG structures using log Bayes factors:

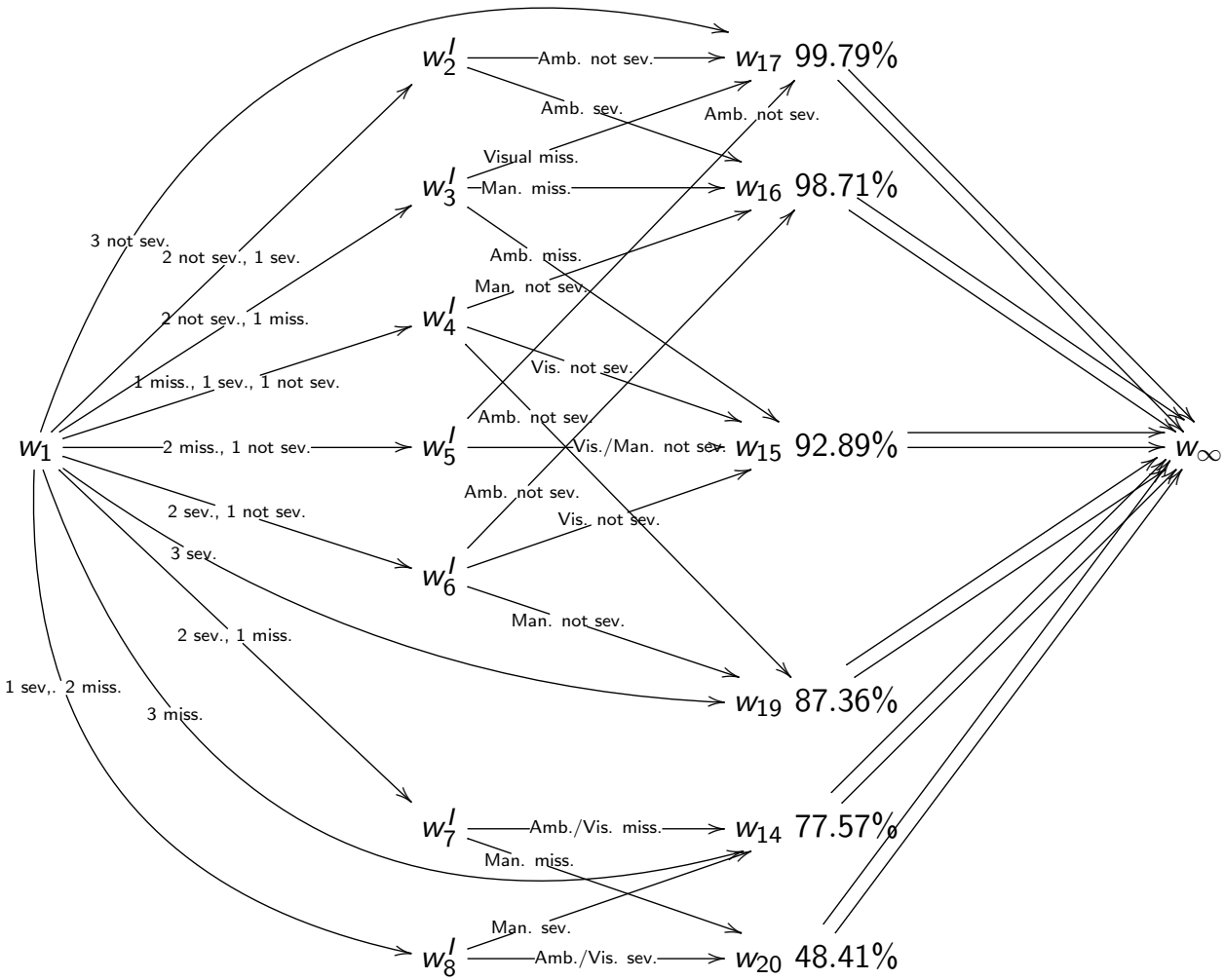
$$log\ L(C_1|D) - log\ L(C_0|D).$$

Model selection: AHC algorithm for CEGs

1. Start with CEG C_0, the finest partition into stages where all leaf nodes of the tree are in the terminal position w_∞ and all other nodes are in separate stages
2. For each pair of situations describing the same variable calculate the log Bayes Factor when putting the two situations into the same stage
3. $C_1 = \arg\max_{C_1^*}(log\ p(D|C_1^*) - log\ p(D|C_0))$, where C_1^* is the CEG constructed by putting two situations into the same stage.
4. Calculate C_2^* by merging two situations in C_1, hence find C_2.
5. Continue until the coarsest partition, C_∞, is reached.
6. Select the CEG of $\{C_0, C_1, C_2, ..., C_\infty\}$ with the highest score.

Default prior distributions are uniform on root to leaf paths.

Reduced CEG for Cerebral Palsy Cohort Study



99.79% (99.63%,99.91%)

98.71% (97.53%,99.51%)

92.89% (90.81%,94.71%)

87.36% (84.17%,90.23%)

77.57% (74.40%,80.59%)

48.41% (31.43%,65.58%)

Missing impairments are associated with poorer survival

Conclusions

- The UK has excellent clinical research in cerebral palsy.
- Predicting the burden of care requires both good data and validated models.
- Exploiting data requires models which allow the effects of variable data quality to be explored.
- The UK has excellent statistical research investigating models for survival, for causal studies and for missing data.