# Causal Inference

a summary

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## 1 Prerequisites

## 1.1 Real Analysis (Abbott, 2015)

Real Numbers  $triangle inequality |a+b| \le |a| + |b|$   $Density \ of \ Q \ in \ R: \ \forall a,b \in \mathbb{R}: \exists r \in \mathbb{Q}: a < r < b$   $Archimedian \ Property: \ \forall x \in \mathbb{R} \ \exists n \in \mathbb{N}: x < n \ \& \ \forall y > 0 \ \exists n \in \mathbb{N}: \frac{1}{n} < y$   $Bounds \ of \ A \subseteq \mathbb{R} \ upper: \ \exists b \in \mathbb{R} \ s.t. \ a \le b \ \forall a \in A \ (lower: \ge)$   $least \ upper \ bound \ (supremum) \ s \in \mathbb{R} \ s.t. \ s \ is \ upper \ bound \ \& \ \forall$   $upper \ bounds \ b: \ s \le b; \ greatest \ lower \ (infimum) \ analogous$   $Cardinality: \ A \sim B, \ if \ \exists f: A \to B, \ where \ f \ bijective \ (in+sur)$   $function \ f: A \to B \ mapping \ f(x) = ..., \ domain = A, \ range \subseteq B$   $in/1-1: \ a_1 \ne a_2 \Rightarrow f(a_1) \ne f(a_2); \ sur/onto: \ if \ \forall b \in B \ \exists a \in A: f(a) = b$ Axiom of  $Completeness: \ every \ nonempty \ set \ of \ real \ numbers$ that is bounded above has a least  $upper \ bound; \ AoC, \ NIP, \ BW,$   $CC, \ MCT \ are \ equivalent: \ if \ one \ is \ assumed \ the \ others \ follow$ Nested  $Interval \ Property: \ if \ I_n = [a_n,b_n] = \{x \in \mathbb{R}: a_n \le x \le b_n\},$ where  $n \in \mathbb{N}$  and  $I_1 \supseteq I_2 \supseteq I_3..., \ then \ \bigcap_{n=1}^{\infty} I_n \ne \emptyset$ 

Sequences are functions with domain  $\mathbb{N}$ Convergence:  $(a_n)$  converges to  $a \in \mathbb{R}$  if  $\forall \epsilon > 0 \exists N \in \mathbb{N}$  s.t.  $n \geq N \Rightarrow |a_n - a| < \epsilon$ ; written as  $\lim a_n = a$  or  $(a_n) \to a$ Cauchy Criterion: sequence converges  $\Leftrightarrow$  is Cauchy sequence Cauchy sequence:  $\forall \epsilon > 0 \exists N \in \mathbb{N}$  s.t.  $m, n \geq N \Rightarrow |a_n - a_m| < \epsilon$ Boundedness:  $(x_n)$  is bounded if  $\exists M > 0$  s.t.  $|x_n| \leq M \, \forall n \in \mathbb{N}$ Algebraic Limit Theorem: if  $(a_n) \to a, (b_n) \to b$ , then  $(ca_n) \to ca, (a_n + b_n) \to a + b, (a_n b_n) \to ab, (a_n / b_n) \to a/b$  for  $b \neq 0$ Order Limit Theorem:  $a_n \geq 0 \, \forall n \in \mathbb{N} \Rightarrow a \geq 0$  ( $\leq$  analogous),  $\exists c \in \mathbb{R}$  s.t.  $c \leq b_n \, \forall n \in \mathbb{N} \Rightarrow c \leq b$  ( $\geq$  analogous)

Monotone Convergence Theorem: bounded & monotone (increasing  $a_n \le a_{n+1}$  or decreasing  $a_n \ge a_{n+1}$ ) sequences converge Bolzano-Weierstrass Theorem:

all bounded sequences have a convergent subsequence subsequences of a convergent sequence converge to the same limit

Series infinite series are sums over sequences:  $\sum_{n=1}^{\infty} b_n$  harmonic series  $\sum_{n=1}^{\infty} \frac{1}{n}$ , geometric series  $\sum_{k=0}^{\infty} ar^k \stackrel{|r| < 1}{=} \frac{a}{1-r}$  Convergence: to B, if  $(s_m) \rightarrow B$ , partial sums  $s_m = \sum_{n=1}^m b_n$  Cauchy Criterion:  $\sum_{k=1}^{\infty} a_k$  converges  $\Leftrightarrow$   $\forall \epsilon > 0 \exists N \in \mathbb{N} \text{ s.t. } n > m \geq N \Rightarrow |a_{m+1} + a_{m+2} + \dots + a_n| < \epsilon$ ; that implies if  $\sum_{k=1}^{\infty} a_k$  converges then  $(a_k) \rightarrow 0$  Algebraic Limit Theorem: if  $\sum_{k=1}^{\infty} a_k = A$  and  $\sum_{k=1}^{\infty} b_k = B$  then  $\sum_{k=1}^{\infty} ca_k = cA$  and  $\sum_{k=1}^{\infty} a_k + b_k = A + B$  Cauchy Condensation Test: if  $(b_n)$  is decreasing and  $b_n \geq 0 \forall n \in \mathbb{N}$  then:  $\sum_{n=0}^{\infty} b_n$  converges  $\Leftrightarrow \sum_{n=0}^{\infty} 2^n b_{2^n}$  converges Comparison Test: if  $0 \leq a_k \leq b_k \forall k \in \mathbb{N}$ , then  $\sum_{k=1}^{\infty} b_k$  converges  $\Rightarrow \sum_{k=1}^{\infty} a_k$  too  $k \geq \sum_{k=1}^{\infty} a_k$  diverges  $k \geq \sum_{k=1}^{\infty} a_k$  too Absolute Convergence Test:  $k \geq \sum_{n=1}^{\infty} |a_n| converges$ , then  $k \geq \sum_{n=1}^{\infty} a_n$  converges

**Absolute Convergence:** if  $\sum_{n=1}^{\infty} |a_n|$  converges then  $\sum_{n=1}^{\infty} a_n$  converges absolutely, if only the latter, then conditionally **Rearrangements:** if  $\sum_{k=1}^{\infty} a_k$  converges absolutely, then any rearrangement converges to the same limit

**Double Series:** if  $\sum_{i=1}^{\infty} \sum_{j=1}^{\infty} |a_{ij}|$  converges  $\Rightarrow \sum_{i=1}^{\infty} \sum_{i=1}^{\infty} a_{ij}$   $= \sum_{j=1}^{\infty} \sum_{i=1}^{\infty} a_{ij} = \lim_{n \to \infty} s_{nn}$ , where  $s_{nn} = \sum_{i=1}^{n} \sum_{j=1}^{n} a_{ij}$ 

Sets Cantor Set:  $C = \bigcap_{n=0}^{\infty} C_n$ , with  $C_n$  removing the middle third of all intervals, e.g.  $C_1 = C_0 \setminus (\frac{1}{3}, \frac{2}{3}) = \left[0, \frac{1}{3}\right] \cup \left[\frac{2}{3}, 1\right]$ Open Sets:  $\forall a \in O \ \exists V_{\epsilon}(a) \subseteq O$ , with  $\epsilon$ -neighborhood of a  $V_{\epsilon}(a) = \{x \in \mathbb{R} : |x - a| < \epsilon\};$  union of open sets is open, the finite intersection of open sets is open

Closed Sets: contain their limit points  $\Leftrightarrow$  every Cauchy sequence has a limit that lies within the set x is  $limit\ point$  of  $A\Leftrightarrow \forall \epsilon>0\ V_\epsilon(x)\cap A$  includes other points than  $x\Leftrightarrow x=\lim(a_n)$  for some  $(a_n)\in A$  with  $a_n\neq x\forall n\in\mathbb{N};$  all non limit point  $a\in A$  are  $isolated\ points;$  the finite union of closed sets is closed, the intersection of closed sets is closed Closure:  $\bar{A}=A\cup L$ , with L the set of A's limit points; the closure is the smallest closed set containing A

Complement:  $A^c = \{x \in \mathbb{R} : x \notin A\}$ ;  $A \text{ closed} \Leftrightarrow A^c \text{ open}$ Compact  $\Leftrightarrow$  Bounded and Closed  $\Leftrightarrow \exists$  Finite Subcover

- Compactness: K compact ⇔ every sequence has a subsequence that converges in K; the intersection of a sequence of nested nonempty compact sets is not empty
- Boundedness:  $\exists M > 0 \text{ s.t. } |a| \leq M \, \forall a \in A$
- Any open cover for A has a finite subcover: An open cover is a set of open sets  $\{O_{\lambda} : \lambda \in \Lambda\}$  whose union contains A; a finite subcover is a finite subset that still covers A

**Perfection:** closed and no isolated points; a nonempty perfect set is uncountable; the Cantor set is perfect

**Separation:** of A and B if  $\bar{A} \cap B = \emptyset$  &  $A \cap \bar{B} = \emptyset$ **Disconnection:** if  $A = B \cup C$ , with B, C nonempty & separated; E is  $connected \Leftrightarrow$  all nonempty disjoint sets B, C s.t.  $E = B \cup C$  have a convergent sequence with a limit in the other set  $\Leftrightarrow$  whenever a < c < b with  $a, b \in E$ , then  $c \in E$ 

Baire's Theorem:  $\mathbb R$  cannot be written as the countable union of nowhere-dense sets; E is nowhere-dense if  $\bar E$  contains no nonempty open intervals

#### Functional Limits and Continuity

**Functional Limit:** let  $f: A \to \mathbb{R}$  and c limit point of A if  $\forall \epsilon > 0 \,\exists \delta > 0 \text{ s.t. } 0 < |x - c| < \delta \text{ (and } x \in A) \text{ it follows}$  $|f(x) - L| < \epsilon$ , then  $\lim_{x \to c} f(x) = L$ Sequential Criterion:  $\lim_{x\to c} f(x) = L \Leftrightarrow \text{for all sequences}$  $(x_n) \subseteq A$ , with  $x \neq c$  and  $(x_n) \to c$  follows  $f(x_n) \to L$ **Algebraic Limit Theorem:** if  $\lim f(x) = L$  and  $\lim g(x) = M$ then  $\lim kf(x) = kL$ ;  $\lim [f(x) + g(x)] = L + M$ ;  $\lim_{x \to \infty} [f(x)g(x)] = LM; \quad \lim_{x \to \infty} f(x)/g(x) = L/M \text{ if } M \neq 0$ **Divergence Criterion:** if  $(x_n)$  and  $(y_n)$  with  $x_n \neq c \neq y_n$  and  $\lim x_n = \lim y_n = c$  but  $\lim f(x_n) \neq f(y_n)$  then  $\not\equiv \lim_{x \to c} f(c)$ Continuity at c:  $\forall \epsilon > 0 \,\exists \delta > 0 \text{ s.t. whenever } |x - c| < \delta \text{ (and }$  $x \in A$ ) then  $|f(x) - f(c)| < \epsilon$ , can also be expressed as:  $(x_n) \to c \text{ (with } x_n \in A) \Rightarrow f(x_n) \to f(c)$ Algebraic Continuity Theorem: if f, g continuous at c then these are too: kf(x), f(x)+g(x), f(x)g(x), f(x)/g(x) (if  $g(x)\neq 0$ ) Compositions: f continuous at c and g is continuous at f(c) $\Rightarrow g \circ f$  is continuous at c (if  $g \circ f(x)$  well-defined) **Boundedness:** f is bounded on its domain  $A \Leftrightarrow f(A)$  is bounded; f is bounded on  $B \subseteq A \Leftrightarrow f(B)$  is bounded **Preservation of Compact Sets:** K compact  $\Rightarrow f(K)$  is too; if f is continuous on a compact set, f attains min/max values **Uniform Continuity:**  $\forall \epsilon > 0 \,\exists \delta > 0 \text{ s.t. whenever } |x - y| < \delta$ 

then  $|f(x) - f(y)| < \epsilon$  (i.e. difference between them is bounded);

f continuous on compact set  $K \Rightarrow f$  uniformly continuous on K

Sequential Criterion for Nonuniformity:  $\exists \epsilon_0 > 0$  and  $(x_n), (y_n)$ 

in A s.t.  $|x_n - y_n| \to 0$  but  $|f(x_n) - f(y_n)| > \epsilon_0$ **Intermediate Value Theorem:**  $f:[a,b]\to\mathbb{R}$  continuous then  $f(a) < L < f(b) \Rightarrow \exists c \in (a, b), \text{ where } f(c) = L$ alternatively: Preservation of Connectedness:  $f: A \to \mathbb{R}$ continuous,  $E \subseteq A$  connected  $\Rightarrow f(E)$  connected Intermediate Value Property (converse of IVM): f has IVP on [a, b] if  $\forall x < y \& L$  s.t.  $f(x) < L < f(y) \exists c \in (x, y)$ , where f(c) = L (implies continuity if f is monotone)

**Discontinuity:** • removable: if  $\lim_{x\to c} f(x)$  exists but  $\neq f(c)$ 

- jump:  $\lim_{x\to c^+} f(x) \neq \lim_{x\to c^-} f(x)$
- essential: not continuous for another reason

The Set of Discontinuous Points  $D_f$  can be written as the countable union of closed sets (=:  $F_{\sigma}$ )

**Derivation**  $g'(c) = \lim_{x \to c} \frac{g(x) - g(c)}{x - c}$  $\begin{array}{ll} (f+g)'(c)=f'(c)+g'(c); & (fg)'(c)=f'(c)g(c)+f(c)g'(c); \\ (kf)'(c)=kf'(c); & (f/g)'(c)=\frac{g(c)f'(c)-f(c)g'(c)}{g^2(c)}, \ \text{for} \ g(c)\neq 0; \end{array}$  $(g \circ f)'(c) = g'(f(c)) \cdot f'(c)$ 

**Differentiability:** Differentiability at c implies continuity at c**Interior Extremum Theorem:** let f differentiable on (a, b); if f has a maximum or minimum at f(c), then f'(c) = 0

**Darboux's Theorem:** if f differentiable on [a, b] and  $f'(a) < \alpha < f'(b)$  then  $\exists c \in (a,b)$ , where  $f'(c) = \alpha$ 

**Rolle's Theorem:**  $f(a) = f(b) \Rightarrow \exists c \in (a,b) \text{ with } f'(c) = 0$ 

**Mean Value Theorem:** if  $f:[a,b] \to \mathbb{R}$  continuous on [a,b] and differentiable on (a,b) then  $\exists c \in (a,b)$  with  $f'(c) = \frac{f(b) - f(a)}{b-c}$ 

Generalized Mean Value Theorem: f, g continuous on [a, b]and differentiable on  $(a,b)\Rightarrow \exists c\in (a,b)$  with [f(b)-f(a)] g'(c)=[g(b)-g(a)] f'(c); if  $g\neq 0:$   $\frac{f'(c)}{g'(c)}=\frac{f(b)-f(a)}{g(b)-g(a)}$ 

L'Hopital's Rules:

**0/0:** let  $a \in I$ , f, g continuous on I, differentiable on  $I \setminus a$ : if f(a)=0=g(a) then  $\lim_{x\to a}\frac{f'(x)}{g'(x)}=L\Rightarrow \lim_{x\to a}\frac{f(x)}{g(x)}=L$   $\infty/\infty$ : let f,g differentiable on (a,b): if  $\lim_{x\to a}g(x)=\infty$  then  $\lim_{x\to a}\frac{f'(x)}{g'(x)}=L\Rightarrow \lim_{x\to a}\frac{f(x)}{g(x)}=L$ 

#### **Functional Sequences**

Convergence: let  $f_n$  be defined on  $A \subseteq \mathbb{R}$ 

Pointwise: if  $\lim_{n\to\infty} f_n(x) = f(x) \ \forall x \in A \text{ then } f_n \to f$ Uniform:  $\forall \epsilon > 0 \,\exists N \in \mathbb{N} \text{ s.t. } |f_n(x) - f(x)| < \epsilon \, \forall x \in A, n \geq N$ Cauchy Criterion:  $(f_n)$  converges uniformly if and only if  $\forall \epsilon > 0 \,\exists N \in \mathbb{N} \text{ s.t. } |f_n(x) - f_m(x)| < \epsilon \,\,\forall x \in A, m, n \geq N$ 

Continuity: let  $(f_n)$  converge uniformly to f, if all  $f_n$  are continuous at  $c \in A$ , then f is in continuous at c

**Differentiability:** let  $(f_n)$  differentiable on [a,b] and  $(f'_n) \to g$ uniformly on [a, b]; if  $\exists x_0 \in [a, b]$  where  $f_n(x_0)$  convergent, then (1)  $(f_n)$  converges uniformly (2)  $f = \lim_{n \to \infty} f_n$  differentiable (3) f' = g

#### Functional Series $\sum_{n=1}^{\infty} f_n(x)$

**Convergence:** converges pointwise (uniformly) on A to f(x) if sequence of partial sums converges pointwise (uniformly) to f(x)Cauchy Criterion:  $\forall \epsilon > 0 \,\exists N \in \mathbb{N} \text{ s.t.}$ 

 $\forall n > m \ge N : |f_{m+1}(x) + f_{m+2}(x) + ... f_n(x)| < \epsilon \, \forall x \in A$ Weierstrass M-Test: let  $(f_n)$  defined on  $A \subseteq \mathbb{R}$ , let  $M_n > 0$ satisfy  $|f_n(x)| \leq M_n \, \forall x \in A$ ; if  $\sum_{n=1}^{\infty} M_n$  converges, then  $\sum_{n=1}^{\infty} f_n$  converges uniformly on A

Power Series:  $f(x) = \sum_{n=0}^{\infty} a_n x^n$ 

Convergence: f(x) converges for  $x_0 \in \mathbb{R} \Rightarrow$  converges absolutely for any x with  $|x| \leq |x_0|$  (the set of convergence is (/[-R,R]/)with  $R \in \mathbb{R}_0^+ \cup \infty$ , R is called the radius of convergence) Abel's Theorem: let f(x) converges at x = R > 0; then f(x)converges uniformly on [0, R] (similar for x = -R);

Uniform Convergence: if a power series converges pointwise on  $A \subseteq \mathbb{R}$ , then it converges uniformly on any compact set  $K \subseteq A$ Differentiability: if f(x) converges on interval  $A \subseteq \mathbb{R}$ , then

- f continuous on A and differentiable on any  $(-R,R) \subseteq A$
- the derivative is  $f'(x) = \sum_{n=1}^{\infty} n a_n x^{n-1}$
- f is infinitely differentiable on (-R, R)

Taylor Series:  $f(x) = \frac{f^{(n)}(a)}{n!}(x-a)^n$  (here a=0)

Lagrange's Remainder Theorem: let f infinitely differentiable on (-R,R), define  $a_n=f^{(n)}(0)/n!$ , let  $S_N$  partial sums to N, then for  $x\neq 0$   $\exists c: |c|<|x|$ , where error  $f(x)-S_N(x)=rac{f^{(N+1)}(c)}{(N+1)!}x^{N+1}$ 

#### Measure Theory (Capiński and Kopp, 2004) 1.2

**Riemann Integral** coinciding upper U and lower L sums for partitions  $P: U = \sum_{i=1}^{n} \sup_{p_i} \operatorname{len}(p_i); L = \sum_{i=1}^{n} \inf_{p_i} \operatorname{len}(p_i)$ **Riemann's Criterion:** f integrable iff  $\forall \epsilon > 0 \,\exists P_{\epsilon} \text{ s.t. } U - L < \epsilon$ Fundamental Theorem of Calculus: if  $f:[a,b] \to \mathbb{R}$ continuous and F' = f, then  $F(b) - F(a) = \int_a^b f(x) dx$ Problems: why do we need a Lebesgue integral?

- $\bullet$  scope: many results need continuous f and bounded intervals
- dependence on intervals: otherwise often not defined
- lack of completeness:  $\int_a^b f_n(x) dx \to \int_a^b f(x) dx$  doesn't hold

Measure  $\mathcal{B} \subset \mathcal{M} \subset \mathcal{P}(\mathbb{R})$ 

**Null Sets**  $\forall \epsilon > 0 \exists$  a sequence of intervals  $(I_n)$  s.t.  $A \subseteq \bigcup_{n=1}^{\infty} I_n$  and  $\sum_{n=1}^{\infty} l(I_n) < \epsilon$  (=  $\exists$  arbitrarily small cover); the union of a sequence of null sets is also null

**Lebesgue Outer Measure** of A:  $m^*(A) = \inf Z_A$ , with  $Z_A = \left\{ \sum_{n=1}^{\infty} l(I_n) : I_n \text{ are intervals, } A \subseteq \bigcup_{n=1}^{\infty} I_n \right\}$ 

- null sets have outer measure zero
- monotonicity:  $A \subset B \Rightarrow m^*(A) \leq m^*(B)$
- the outer measure of an interval equals its length
- countable subadditivity:  $m^* \left( \bigcup_{n=1}^{\infty} E_n \right) \leq \sum_{n=1}^{\infty} m^*(E_n)$
- translation invariance:  $m^*(A) = m^*(A+t)$

**Lebesgue Measurability:** of  $E \subseteq \mathbb{R}$  (write  $E \in \mathcal{M}$ ) if  $\forall A \subseteq \mathbb{R} : m^*(A) = m^*(A \cap E) + m^*(A \cap E^c)$  (additivity)  $\mathcal{M}$  is a  $\sigma$ -field: and countably additive (=: measure)

- $\mathbb{R} \in \mathcal{M}$  (btw so are all null sets and intervals)
- $E \in \mathcal{M} \Rightarrow E^c \in \mathcal{M}$
- $E_n \in \mathcal{M} \, \forall n \Rightarrow \bigcup_{n=1}^{\infty} E_n \in \mathcal{M}$ , with countable additivity:  $m^*(\bigcup_{n=1}^{\infty} E_n) = \sum_{n=1}^{\infty} m^*(E_n)$  for  $E_j \cap E_k = \emptyset$  if  $j \neq k$ (it follows that  $\mathcal{M}$  is closed under countable intersections as well) the intersection of  $\sigma$ -fields is a  $\sigma$ -fields

Open Sets: every open set in  $\mathbb{R}$  can be expressed as a union of countable open intervals  $\Rightarrow$  all open sets are in  $\mathcal{M}$ 

**Lebesgue Measure**  $m: f: \mathcal{M} \to [0, \infty]$ , countably additive  $m^*$ 

- let  $A_n \in \mathcal{M} : A_n \subset A_{n+1} \forall n \Rightarrow m(\bigcup_n A_n) = \lim_n m(A_n)$ let  $m(A_n) < \infty : A_n \supset A_{n+1} \forall n \Rightarrow m(\bigcap_n A_n) = \lim_{n \to \infty} m(A_n)$
- m is continuous at  $\emptyset$ , i.e.  $(B_n)$  decrease to  $\emptyset \Rightarrow m(B_n) \to 0$

Borel Sets:  $\sigma$ -field generated by a family of sets

 $\mathcal{B} = \bigcap \{ \mathcal{F} : \mathcal{F} \text{ is a } \sigma\text{-field containing all intervals} \}$ 

 ${\mathcal B}$  is also generated by intervals of a particular type Completion: not all null sets are in  $\mathcal{B}$ 

 $\mathcal{M}$  is the completion of  $\mathcal{B}$ : a measure space  $(X, \mathcal{F}, \mu)$  is complete if  $\forall F \in \mathcal{F}$  with  $\mu(F) = 0$ :  $N \subset F$  is in  $\mathcal{F}$  and  $\mu(N) = 0$ 

Borel Regular Measure:  $\mu(B) = \inf\{\mu(O) : O \text{ open}, O \supset B\} = \sup\{\mu(F) : F \text{ closed}, F \supset B\}; Approximations: of } m \text{ for } E \in \mathcal{M}$  above:  $\forall \epsilon > 0 \exists \text{ open set } O \text{ s.t. } A \subset O, m(O) \leq m^*(A) + \epsilon$  below: if  $E \in \mathcal{M}$  then  $\epsilon > 0 \exists \text{ closed set } F \subset E \text{ s.t. } m(E \setminus F) < \epsilon$  **Probability** restriction to  $\mathcal{M}_B = \{A \cap B : A \in \mathcal{M}\}$  Probability Space:  $(\Omega, \mathcal{F}, P)$ , with  $\Omega$  an arbitrary set,  $\mathcal{F}$  a  $\sigma$ -field of subsets of  $\Omega$  called events, and P measure on  $\mathcal{F}$  s.t.  $P(\Omega) = 1$ ; Independence:

• events  $E = \{A_1, ...A_n\}$ :  $\forall K \subseteq E : P(\bigcap_K A_i) = \prod_K P(A_i)$ •  $\sigma$ -fields  $S = \{\mathcal{F}_1, ...\mathcal{F}_n\}$  on  $(\Omega, \mathcal{F}, P)$ :  $\forall S_s \subseteq S : F_i \in \mathcal{F}_j \in S_s \Rightarrow P(\bigcap_{S_s} F_i) = \prod_{S_s} P(F_i)$ 

Measurable Functions define f only up to null sets (a.e.) **Extended**  $\mathbb{R}$ :  $\mathbb{R} = [-\infty, \infty]$ , with  $0 \cdot \infty = 0$  and avoid  $\infty - \infty$ (Lebesgue) Measurability: target range (Riemann: domain) E is measurable,  $f: E \to \mathbb{R}$  is measurable if  $\forall I \subseteq \mathbb{R}$ :  $f^{-1}(I) \in \mathcal{M}$  (if  $\in \mathcal{B}$ , then Borel(-measurable) function) Equivalences: f is measurable  $\Leftrightarrow \forall a : f^{-1}(x)$  is measurable for x in  $\{(a, \infty), [a, \infty), (-\infty, a), (-\infty, a]\}$ Measurable f: constant, continuous (due to open sets), monotone **Properties:** m'able  $f: E \rightarrow \mathbb{R}$ : vector space, i.e. f+q, fq m'able  $F: \mathbb{R} \times \mathbb{R} \to \mathbb{R}$  continuous and f, g m'able  $\Rightarrow F(f(x), g(x))$  m'able  $f^-, f^+$  m'able  $\Leftrightarrow f$  m'able  $\Rightarrow |f|$  m'able  $(f_n)$ m'able  $\Rightarrow \max_{n \leq k} f_n, \sup_{n \in N} f_n, \lim \sup_{n \to \infty} f_n$ m'able (also min etc.)  $f, g: E \rightarrow \mathbb{R}, E \in \mathcal{M}, f$  m'able,  $\{x: f(x) = g(x)\}$  null  $\Rightarrow g$  m'able  $(f_n)$  m'able,  $f_n(x) \to f(x)$  a.e. for  $x \in E \Rightarrow f$  m'able **Essential Supremum:** ess sup  $f := \inf\{z : f \le z \text{ a.e.}\}$  (also inf) **Probability** random variable m'able  $X: \Omega \to \mathbb{R}$  $\sigma$ -field gen. by  $X: X^{-1}(\mathcal{B}) = \{S \in \mathcal{F} : S = X^{-1}(B) \text{ for some } B \in \mathcal{B}\}$ probability distribution:  $P_X(B) = P(X^{-1}(B))$  is count. add. Dirac measure:  $\delta_a(B) = \mathbb{1}(a \in B)$  $X, Y \ indep.: \ \forall B, C \ in \ \mathbb{R}: X^{-1}(B) \perp \!\!\!\perp Y^{-1}(C)$ 

**Integral** over  $E \in \mathcal{M}$  with measure  $m: \int_E f \, dm$ on simple function  $\varphi$  (range is finite set of reals  $a_i > 0$ , with corresp. domain m'able  $A_i$ ):  $\int_E \varphi \, dm = \sum_{i=1}^n a_i m(A_i \cap E)$ on m'able function  $f \ge 0$ :  $\int_E f \, dm = \sup Y(E, f)$ , where  $Y(E,f) = \big\{ \int_E \varphi \, \mathrm{d} m : 0 \le \varphi \le f, \varphi \text{ is simple} \big\}; \, f = 0 \text{ a.e.} \Leftrightarrow \int f \, \mathrm{d} m$ Monotone Convergence Theorem if  $\{f_n\} \geq 0$ , m'able, &  $f_n \to f$  then:  $\lim_{n \to \infty} \int_E f_n(x) dm = \int_E f dm$ (if limit is only a.e. then E has to be m'able for result to hold) on m'able function f:  $\int_E f dm = \int_E f^+ dm - \int_E f^- dm$ (f is only integrable if both components are finite)set of all functions that are integrable over E is called  $\mathcal{L}^1(E)$ **Properties:** let f, g integrable,  $c \in \mathbb{R}$ , A, E measurable then  $f \le g \Rightarrow \int f \, dm \le \int g \, dm; \int (cf) \, dm = c \int_E f \, dm;$ f+g int'able,  $\mathcal{L}^1$  vector space;  $\int_E (f+g)\,\mathrm{d}m = \int_E f\,\mathrm{d}m + \int_E g\,\mathrm{d}m;$  $\int_A f \, \mathrm{d}m \le \int g \, \mathrm{d}m \forall A \Rightarrow f \le g$  a.e.; int'able f is finite a.e.;  $m(A)\inf_A f \leq \int_A f \, dm \leq m(A)\sup_A f$ ;  $|\int f \, dm| \leq \int |f| \, dm$ ; let  $f \ge 0$ : (1)  $\int f dm = 0 \Rightarrow f = 0$  a.e. (2)  $A \to \int_A f dm$  is measure Dominated Convergence Theorem:  $(f_n)$  measurable,  $|f_n| \leq g$ a.e. on  $E \in \mathcal{M}$ , g E-int'able  $\Rightarrow \lim_{n \to \infty} \int_E f_n(x) \, \mathrm{d}m = \int_E f \, \mathrm{d}m$   $Beppo-Levi: \sum_{n=1}^{\infty} \int |f_n| \, \mathrm{d}m$  finite  $\Rightarrow \sum_{n=1}^{\infty} f_n(x)$  converges a.e., is integrable and  $\int \sum_{n=1}^{\infty} f_n dm = \sum_{n=0}^{\infty} \int f_n dm$ Relation to Riemann integrals: let  $[a, b] \to \mathbb{R}$  bounded f continuous a.e.  $\Leftrightarrow f$  is R-int'able  $\Rightarrow f$  is L-int'able  $(F_R = F_L)$ L-int's also equal improper R-int's (e.g.  $\lim_{a \to -\infty, b \to \infty} \int_{-b}^{b} f(x)dx$ )

f on [a,b] bounded:  $\forall \epsilon > 0 \exists$  step function h s.t.  $\int_a^b |f-h| dm \le \epsilon$ 

 $f \in \mathcal{L}^1$ :  $\forall \epsilon > 0 \exists g \text{ (cont's, zero outside int.) s.t. } \int |f-h| dm \leq \epsilon$ 

Approximating m'able functions:

Riemann-Lebesgue:  $f \in \mathcal{L}^1$ :  $s_n = \int_{-\infty}^{\infty} f(x) \sin(kx) \, \mathrm{d}x$  go to 0 **Probability**: for r.v. X:  $\int_{\Omega} g(X(\omega)) \, \mathrm{d}P(\omega) = \int_{\mathbb{R}} g(x) \, \mathrm{d}P_X(x)$  absolutely continuous: int'able  $f \geq 0$ , where measure  $A \to P(A) = \int_A f \, \mathrm{d}m$ ; f is called a density with  $\int f \, \mathrm{d}m = 1$ ; cdf: defined as  $F(y) = P_X((-\infty, y]) \stackrel{a.c.}{=} \int_{-\infty}^y f(x) \, \mathrm{d}x$ , continuity of F does not imply f exists (see Lebesgue function),  $F_X$  is 1 non-decreasing, 2 right continuous and 3 goes from 0 to 1,  $g: \mathbb{R} \to \mathbb{R}$  increasing & diff'able:  $f_{g(X)}(y) = f_X(g^{-1}(y)) \frac{\mathrm{d}}{\mathrm{d}y} g^{-1}(y)$  Expectation:  $\mathbb{E}(X) = \int_{\Omega} X \, \mathrm{d}P = \int x \, \mathrm{d}P_X(x) \stackrel{a.c.}{=} \int x f_X(x) \, \mathrm{d}x$   $\mathbb{C}$ :  $\int_E u + \mathrm{i}v \, \mathrm{d}m = \int_E u \, \mathrm{d}m + \mathrm{i} \int_E v \, \mathrm{d}m$ ,  $|\int_E f \, \mathrm{d}m| \leq \int_E |f| \, \mathrm{d}m$  Characteristic Function:  $\varphi_X(t) = \mathbb{E}(\exp^{\mathrm{i}tX}) = \int \exp^{\mathrm{i}tx} \, \mathrm{d}P_X(x)$  for r.v. X, with  $t \in \mathbb{R}$ ;  $\varphi_X(0) = 1$ ,  $-1 \leq \varphi_X(t) \leq 1$ 

Spaces Of Integrable f  $\infty$ -dim. normed vector spaces  $L^1$  (Banach space := complete normed space): **norm:**  $x \to ||x||$ , with  $x \in \text{vector space: } ||x|| \ge 0$ ,  $||x|| = 0 \Leftrightarrow x = 0, ||\alpha x|| = |\alpha| ||x|| \ (\alpha \in \mathbb{R}/\mathbb{C}), \text{ triangle equality}$ **metric:**  $d: X \times X \to \mathbb{R}$  (X set), with  $d(x,y) \geq 0$ , symmetric,  $d(x,y)=0 \Leftrightarrow x=y$ , triangle equality; e.g.:  $d(x,y)=\|x-y\|$ consider vector space  $L^1(E) = \mathcal{L}^1(E)/_{\sim}$ , where  $f \sim g \Leftrightarrow$ f(x) = g(x) a.e. with  $||f||_1 = \int_E |f| dm$ ,  $L^1(E)$  is complete  $L^2$  (Hilbert space := Banach space + (.,.) inducing ||.||):  $\mathcal{L}^2$  is set of m'able functions where norm  $||f||_2 = (\int_E |f|^2 dm)^{\frac{1}{2}}$ is finite, with  $L^2$  its set of equivalence classes norm fulfills  $\Delta$ -eq. due Schwarz Inequality:  $f, g \in L^2(E, \mathbb{C}) \Rightarrow$  $|\int_E f\bar{g}\,\mathrm{d}m| \leq \|fg\|_1 \leq \|f\|_2 \|g\|_2$  (\$\bar{g}\$ complex conjugate: \$a-bi\$)  $L^1 \not\subset \mathcal{I}$  L<sup>2</sup>, but if for set D:  $m(D) < \infty$  then  $L^2(D) \subset L^1(D)$ inner product:  $(f,g) := \int f\bar{g} \,dm$  (induces  $\|.\|_2$ ) *inner product:*  $(.,.): H \times H \to \mathbb{C}$ , which is (with induced norm) • linear (1st .): (f+g,h) = (f,h) + (g,h), (cf,h) = c(f,h)• conjugate symmetric:  $(f,g) = \overline{(g,f)}$ • positive definite:  $(f,f) \ge 0, (f,f) = 0 \Leftrightarrow f = 0$ • (if  $\mathbb{C}$ : conjugate) linear (2nd .):  $(f, cg + h) = \bar{c}(f, g) + (f, h)$  $\rightarrow parallelogram\ law:\ \|f+g\|^2 + \|f-g\|^2 = 2\|f\|^2 + 2\|g\|^2$  $\rightarrow \textit{polar.: } 4(f,g) = \|f+g\|^2 - \|f-g\|^2 + \mathrm{i} \left(\|f+\mathrm{i} g\|^2 - \|f-\mathrm{i} g\|^2\right)$ orthogonal: (f,g) = 0, angle:  $\cos \theta = \frac{(f,g)}{\|f\| \|h\|} = \text{correlation}$  $||h - h'|| = \inf\{||h - k|| : k \in K\}$ \*Decomposition:  $\forall h \in H : h = h' + h''$ , where h' orthogonal projection on K (complete subspace of H) and h'' orthogonal to K. Therefore  $H = K \oplus K^{\perp}$  (all  $k \in K$  orthogonal to all  $k' \in K^{\perp}$ ).  $\pmb{L^p}$  (Banach spaces): E Lebesgue-finite,  $p \leq q \Rightarrow L^q(E) \subseteq L^p(E)$ for  $1 \le p \le \infty$ :  $||f||_p = (\int_E |f|^p dm)^{\frac{1}{p}}$ ;  $||f||_{\infty} = \text{ess sup } f$  $\mbox{\emph{H\"older's Inequality}}$  (needed for  $\Delta$  eq.; generalizes Schwarz): let  $\frac{1}{p} + \frac{1}{q} = 1$ ,  $f \in L^p$ ,  $g \in L^q \Rightarrow fg \in L^1$  and  $||fg||_1 \le ||f||_p ||g||_q$ Minkowski's Inequality:  $f, g \in L^p \Rightarrow ||f+g||_p \leq ||f||_p + ||g||_p$ **Probability:** nth moment:  $\mathbb{E}(X^n)$ , central moment:  $\mathbb{E}(X-\mu)^n$  $\mathbb{E}(X^n)$  (in)finite  $\Rightarrow \mathbb{E}(X^k)$  (in)finite  $(k \leq n)$ ; moments (c.m.) of order n are determined by c.m. (moments) of order k for  $k \leq n$  $\mathbb{E}(X^k) = \frac{1}{i^k} \frac{\mathrm{d}^k}{\mathrm{d}t^k} \varphi_X(0)$  (if kth moment finite,  $\varphi_X$  is  $k \times$  diff'able) independent:  $\mathbb{E}(f(X)g(Y)) = \mathbb{E}(f(X))\mathbb{E}(g(Y)), f, g \text{ bounded } \mathcal{B}\text{-m}$  $\mathbb{E}(XY) = (X, Y)$ , it follows:  $Cov(X, Y) = (X_c, Y_c) =$  $\mathbb{E}((X - \mathbb{E}(X))(Y - \mathbb{E}(Y)))$ , where  $X_c = X - \mathbb{E}(X)$  centered r.v.  $\operatorname{Var}(\sum X_i) = \sum \operatorname{Var}(X_i); \, \varphi_{X_1 + \dots + X_n}(t) = \varphi_{X_1}(t) \cdots \varphi_{X_n}(t)$ Conditional Expectation: let  $(\Omega, \mathcal{F}, P)$  where  $\mathcal{G}$  is sub- $\sigma$ -field of  $\mathcal{F}$ , if  $X \in \mathcal{L}^1(\mathcal{F}) \ \exists Y \in \mathcal{L}^1(\mathcal{G})$  s.t.  $\int_G Y \, \mathrm{d}P = \int_G X \, \mathrm{d}P \ \forall G \in \mathcal{G}$  $Y = \mathbb{E}(X|\mathcal{G})$  is uniquely defined up to P-null sets construct Y when  $X \in \mathcal{L}^2$ : Y as orthogonal projection to  $K = L^2(\mathcal{G}) \text{ (see *)} \Rightarrow (X - Y, \mathbb{1}_G) = 0 \text{ as } \mathbb{1}_G \in L^2(\mathcal{G}) \ \forall G \in \mathcal{G}$  $\rightarrow$  can be seen as minimising distance between X and  $\mathcal{L}^2(\mathcal{G})$  $\to Y$  is 'best predictor' of X in  $\mathcal{L}^2(\mathcal{G})$ 

Product Measures  $\mathbb{R}^n$ : cubes  $I = I_1 \times ... \times I_n$  with length  $l(I) = l(I_1) \times ... \times l(I_n)$ , where hyperplanes are null sets Product σ-fields: from measure spaces  $(\Omega_i, \mathcal{F}_i, P_i)$ :  $(\Omega, \mathcal{F}, P)$  with  $\Omega = \Omega_1 \times \Omega_2$  and  $\mathcal{F}$  generated by rectangles  $\mathcal{R} = \{A_1 \times A_2 : A_1 \in \mathcal{F}_1, A_2 \in \mathcal{F}_2\}$ , write  $\mathcal{F} = \mathcal{F}_1 \times \mathcal{F}_2$  Measure:  $P = P_1 \times P_2$ , with σ-finite  $P_i$ , i.e.  $\exists (A_n) : \bigcup_{n=1}^{\infty} A_n = \Omega_i$ , with  $P_i(A_n)$  finite;  $P(A) = \int_{\Omega_2} P_1(A_{\omega_2}) \, \mathrm{d}P_2(\omega_2)$  with section  $A_{\omega_2} = \{\omega_1 \in \Omega_1 : (\omega_1, \omega_2) \in A\} \subset \Omega_1$  and measurable function  $\omega_2 \to P_1(A_{\omega_2}) = \mathbb{I}_{\omega_2 \in A} P(A_1)$  fulfills  $P(A_1 \times A_2) = P_1(A_1) P_2(A_2)$  and P is countably additive

fulfills  $P(A_1 \times A_2) = P_1(A_1)P_2(A_2)$  and P is countably additive **Fubini's Theorem:** integrate  $f \in L^1(\Omega_1 \times \Omega_2)$  over sections  $\omega_1 \to \int_{\Omega_2} f(\omega_1, \omega_2) dP_2(\omega_2)$  ( $\omega_2$  analogous)

$$\int_{\Omega_1 \times \Omega_2} f \, \mathrm{d}(P_1 \times P_2) = \int_{\Omega_1} \left( \int_{\Omega_2} f \, \mathrm{d}P_2 \right) \mathrm{d}P_1$$
**Probability** random vector  $(X,Y) : \Omega \to \mathbb{R}$ 

joint density: if  $\exists f_{(X,Y)}: P_{(X,Y)}(B) = \int_B f_{(X,Y)}(x,y) \, \mathrm{d} m_2(x,y)$  marginal distributions: if X,Y have a joint density, they are absolutely continuous with  $f_X(x) = \int_{\mathbb{R}} f_{(X,Y)}(x,y) \, \mathrm{d} y$  independence: iff  $P_{(X,Y)} = P_X \times P_Y$  or if  $\exists$  joint density:

$$\begin{split} &f_{(X,Y)}(x,y) = f_X(x) \times f_Y(y) \\ &X + Y \colon f_{X+Y}(z) = \int_{\mathbb{R}} f_{X,Y}(x,z-x) \, \mathrm{d}x \stackrel{\coprod}{=} \int_{\mathbb{R}} f_X(x) f_Y(z-x) \, \mathrm{d}x \\ &characteristic \ function \colon \text{if} \ F_X \ \text{continuous} \ \text{at} \ a,b \in \mathbb{R} : \\ &F_X(b) - F_X(a) = \lim_{c \to \infty} \frac{1}{2\pi} \int_{-c}^c \frac{\exp^{-\mathrm{i} u a} - \exp^{\mathrm{i} u b}}{\mathrm{i} u} \varphi_X(u) \, \mathrm{d}u; \\ &\text{if} \ \varphi_X \ \text{integrable:} \ f_X(x) = \frac{1}{2\pi} \int_{-\infty}^\infty \exp^{-\mathrm{i} u x} \varphi_X(x) \, \mathrm{d}u \end{split}$$

Radon-Nikodym  $(\Omega, \mathcal{F})$  is a measurable space absolute continuity  $(\nu \ll \mu)$ : if  $\mu(A)=0 \Rightarrow \nu(A)=0 \ \forall A \in \mathcal{F}$ ,  $\nu \ll \mu$  iff:  $\forall \epsilon > 0 \ \exists \delta > 0 \ \text{s.t.} \ \mu(F) < \delta \Rightarrow \nu(F) < \epsilon \ \forall F \in \mathcal{F}$  Radon-Nikodym:  $\nu, \mu$   $\sigma$ -finite,  $\nu \ll \mu$ :  $\exists$  m'able function  $\geq 0$   $h: \Omega \to \mathbb{R}$  s.t.  $\nu(F)=\int_F h \ \mathrm{d}\mu \ \forall F \in \mathcal{F}$ , h is unique up to  $\mu$ -null sets Radon-Nikodym derivative:  $\frac{\mathrm{d}\nu}{\mathrm{d}\mu}=h$  with  $\lambda \ll \mu, \ \nu \ll \mu$  implying  $\phi = \lambda + \nu \Rightarrow \frac{\mathrm{d}\phi}{\mathrm{d}\mu} = \frac{\mathrm{d}\lambda}{\mathrm{d}\mu} + \frac{\mathrm{d}\nu}{\mathrm{d}\mu}$  a.s. and  $\lambda \ll \nu \Rightarrow \frac{\mathrm{d}\lambda}{\mathrm{d}\mu} = \frac{\mathrm{d}\lambda}{\mathrm{d}\nu} \frac{\mathrm{d}\mu}{\mathrm{d}\mu}$  a.s. mutual singularity  $(\mu \perp \nu)$ : concentrated on disjoint  $A_i \in \Omega$ 

 $\lambda$  concentrated on  $E \in \mathcal{F}$ :  $\lambda(F) = \lambda(E \cap F) \ \forall F \in \mathcal{F}$ **Lebesgue decomposition:**  $\lambda = \lambda_a + \lambda_s$ , where  $\lambda_a \ll \mu$  and  $\lambda_s \perp \mu$  $\lambda(E) = \int_E h \, d\mu + \lambda_s(E)$  "linear combination":  $\mu$  acting as "basis" Lebesgue-Stieltjes measure: distribution function F has only jump discontinuities & is right continuous, i.e. F(x+) = F(x)F-outer measure  $m_F^*$ :  $m^*$  using  $l_F$  on intervals, restricted to  $\mathcal{M}_F$ : complete, contains  $\mathcal{B}$  but  $\neq \mathcal{M}$ , if F(x) = x then  $m_F = m$ absolute continuity of real function F on [a, b] if  $\forall \epsilon > 0 \; \exists \, \delta > 0 \; \text{s.t.} \; \forall \; \text{sets of} \; n \; \text{disjoint} \; J_k = (x_k, y_k) \; \text{in} \; [a, b] \; \text{with}$  $\sum_{k=1}^{n} (y_k - x_k) < \delta$  follows  $\sum_{k=1}^{n} |F(x_k) - F(y_k)| < \epsilon$ ; F monotone increasing & absolutely continuous  $\Rightarrow$  every Lebesgue-measurable set is  $m_F$ -measurable and  $m_F \ll m$ bounded variation  $(F \in BV[a, b])$  if  $T_F[a, b] < \infty$  where  $T_F[a,x] = \sup\{\sum_{k=1}^n |F(x_k) - F(x_{k-1})|\} \Leftrightarrow \text{ is the difference of }$ two monotone increasing real functions on [a, b]; absolutely continuous functions are  $\in BV[a,b]$  as well as the components of the minimal decomposition  $F = F_1 - F_2$ , Lebesgue-Stieltjes signed measure of F  $m_F = m_{F_1} - m_{F_2}$  on  $\mathcal B$ signed measure:  $\nu: \mathcal{F} \to (-\infty, +\infty]$  with  $\nu(\emptyset) = 0$  and countably additive,  $\nu$  monotone increasing  $\Rightarrow$  is measure; total variation  $|\nu|$  of a bounded signed measure is a measure,  $\nu^{+(-)} = \frac{1}{2}(|\nu|+(-)\nu)$ ; with  $\mu$  measure: unique  $\nu = \nu_a + \nu_s$  with  $nu_a \ll \mu \& \nu_s \perp \!\!\!\perp \mu$  and  $\nu_a(F = \int_F h \, \mathrm{d}\mu \, \forall F \in \mathcal{F} \text{ with } h \in \mathcal{L}^1(\mu);$  $\nu$  bounded signed measure and  $F(x) = \nu((-\infty, x])$  then: Fdiff'able with  $F'(a) = L \Leftrightarrow \forall \epsilon > 0 \; \exists \; \delta > 0 \; \text{s.t.} \; |\frac{\nu(J)}{\mu(J)} - L| < \epsilon \; \text{if open}$ interval J around a and  $l(J) < \epsilon$ 

Fundamental Theorem of Calculus: F absolutely continuous on [a,b] then F is diff'able m-a.e.,  $\frac{\mathrm{d} m_F}{\mathrm{d} m} = F'$ , and  $F(x) - F(a) = m_F[a,x] = \int_a^x F'(t) \, \mathrm{d}t \ \, \forall x \in [a,b]$  Hahn-Jordan decomposition:  $\nu$  bounded signed measure

**Hahn-Jordan decomposition:**  $\nu$  bounded signed measure then disjoint  $A \cup B = \Omega$  with  $\nu^{+(-)}(F) = \nu(B(A) \cap F) \ \forall F \in \mathcal{F}$ , if  $\nu = \lambda_1 - \lambda_2$  then  $\lambda_1 \geq \nu^+$ ,  $\lambda_2 \geq \nu^-$ 

integrals of signed measures:  $\int_F f \, \mathrm{d}\mu = \int_F f \, \mathrm{d}\mu^+ - \int_F f \, \mathrm{d}\mu^-$  (whenever this ist not  $\pm (\infty - \infty)$ )

## 2 General

#### Ladder Of Causation (Pearl, 2019)

1. rung: **association** Pr[y|x] observation What is? 2. rung: **intervention** Pr[y|do(x), z] experiment What if? 3. rung: **counterfactuals**  $Pr[y^x|x', y']$  retrospection Why? if a tool can answer rung i questions, it can also answer rung j < i

Causal Roadmap (Petersen and van der Laan, 2014) systematic approach linking causality to statistical procedures

- 1. Specifying Knowledge. structural causal model (unifying counterfactual language, structural equations, & causal graphs): a set of possible data-generating processes, expresses background knowledge and its limits
- 2. Linking Data. specifying measured variables and sampling specifics (latter can be incorporated into the model)
- ${\bf 3. \ Specifying \ Target.} \ {\bf define \ hypothetical \ experiment: \ decide}$ 
  - 1. variables to intervene on: one (point treatment), multiple (longitudinal, censoring/missing, (in)direct effects)
  - 2. intervention scheme: static, dynamic, stochastic
  - counterfactual summary of interest: absolute or relative, marginal structural models, interaction, effect modification
  - 4. population of interest: whole, subset, different population
- **4. Assessing Identifiability.** are knowledge and data sufficient to derive estimand and if not, what else is needed?
- **5. Select Estimand.** current best answer: knowledge-based assumptions + which minimal convenience-based asspumptions (transparency) gets as close as possible
- **6. Estimate.** choose estimator by statistical properties, nothing causal here
- 7. Interpret. hierarchy: statistical, counterfactual, feasible intervention, randomized trial

Average Causal Effect  $E[Y^{a=1}] \neq E[Y^{a=0}]$ 

$$\begin{split} & \mathbf{E}\left[Y^{a}\right] = \sum_{y} y p_{Y^{a}}(y) & \text{(discrete)} \\ & = \int y f_{Y^{a}}(y) dy & \text{(continuous)} \end{split}$$

individual causal effect  $Y_i^{a=1} \neq Y_i^{a=0}$  generally unidentifiable  $null\ hypothesis$ : no average causal effect  $sharp\ null\ hypothesis$ : no causal effect for any individual  $notation\ A,Y$ : random variables (differ for individuals); a,y: particular values; counterfactual  $Y^{a=1}$ : Y under treatment a=1  $stable\ unit\ treatment\ value\ assumption\ (SUTVA)\ Y_i^a$  is well-defined: no interference between individuals, no multiple versions of treatment (weaker: treatment variation irrelevance)  $causal\ effect\ measures\ typically\ based\ on\ means$ 

risk difference: 
$$\Pr[Y^{a=1}=1] - \Pr[Y^{a=0}=1]$$
  
risk ratio:  $\frac{\Pr[Y^{a=1}=1]}{\Pr[Y^{a=0}=1]}$   
odds ratio:  $\frac{\Pr[Y^{a=1}=1]/\Pr[Y^{a=1}=0]}{\Pr[Y^{a=0}=1]/\Pr[Y^{a=0}=0]}$ 

number needed to treat (NNT) to save 1 life: -1/risk difference sources of random error: sampling variability (use consistent estimators), nondeterministic counterfactuals association compares E[Y|A=1] and E[Y|A=0], causation

association compares E[Y|A=1] and E[Y|A=0], causation compares  $E[Y^{a=1}]$  and  $E[Y^{a=0}]$  (whole population)

Target Trial emulating an ideal randomized experiment explicitly formulate target trial & show how it is emulated  $\rightarrow$  less vague causal question, helps spot issues missing data problem unknown counterfactuals

randomized experiments: missing completely at random  $\rightarrow$  exchangeability (= exogeneity as treatment is exogenous) ideal randomized experiment: no censoring, double-blind, well-defined treatment, & adherence  $\rightarrow$  association is causation pragmatic trial: no placebo/blindness, realistic monitoring **PICO** (population, intervention, comparator, outcome): some components of target trial

#### three types of causal effects:

intention-to-treat effect (effect of treatment assignment)
per-protocol effect (usually dynamic when toxicity arises)
other intervention effect (strategy changed during follow-up)

**controlled direct effects:** effect of A on Y not through B natural direct effect A on Y if  $B^{a=0}$  (cross-world quantity) principal stratum effect A on Y for subset with  $B^{a=0} = B^{a=1}$ 

crossover experiment: sequential treatment & outcome t=0, 1 individual causal effect  $Y_{it}^{a_t=1} - Y_{it}^{a_t=0}$  only identifiable if: no carryover effect, effect  $\bot$  time, outcome  $\bot$  time time zero if eligibility at multiple t (observational data): earliest, random t, all t (adjust variance with bootstrapping) grace periods: usually treatment starts x months after first eligible, if death before: randomly assign strategy/copy into both

**Identifiability Conditions** hold in ideal experiments **consistency** counterfactuals correspond to data  $Y = Y^A$ : if A = a, then  $Y^a = Y$  for each individual

- precise definition of Y<sup>a</sup> via specifying a (sufficiently well-defined a maybe impossible (effect of DNA before it was discovered), relies on expert consensus)
- linkage of counterfactuals to data (a must be seen in data)  $\begin{aligned} \textbf{positivity} \ \Pr\left[A=a|L=l\right] > 0 \ \ \forall \, l \ \text{with} \ \Pr\left[L=l\right] > 0; \\ f_L(l) \neq 0 \Rightarrow f_{A|L}(a|l) > 0 \ \forall a, l \end{aligned}$
- $\bullet\,$  structural violations (inference not on full population)
- random variability (smooth over with parametric models) can sometimes be empirically verified (if all is seen in data) **exchangeability** unverifiable without randomization
- marginal:  $Y^a \perp \!\!\! \perp A \cong$  randomized experiment, counterfactuals are missing completely at random (MCAR)
- conditional:  $Y^a \perp \!\!\! \perp A | L \ \widehat{=} \$  conditionally randomized, counterfactuals are missing at random (MAR) alternative definition:  $\Pr \left[ A = 1 | Y^{a=0}, L \right] = \Pr \left[ A = 1 | L \right]$  additional conditions:

correct measurement mismeasurement of A,Y,L results in bias correct model specification models  $\overset{\text{may}}{\to}$  misspecification bias

Effect Modification A on Y varies across levels of V null average causal effect  $\neq$  null causal effect per subgroup population characteristics: causal effect measure is actually "effect in a population with a particular mix of effect modifiers" transportability: extrapolation of effect to another population (issues: effect modification, versions of treatment, interference) effects conditional on V may be more transportable types: additive/multiplicative scale, qualitative (effect in opposite directions)/quantitative, surrogate/causal calculation:

- ullet stratify by V then standardize/IP weight for L,
- L as matching factor (ensures positivity, difficult if high-dimensional L)

**collapsibility:** causal risk difference and ratio are weighted averages of stratum-specific risks, can not be done for odds ratio

**Interaction** effects of joint interventions A and E

$$\Pr\left[Y^{1,1}{=}1\right] - \Pr\left[Y^{0,1}{=}1\right] \neq \Pr\left[Y^{1,0}{=}1\right] - \Pr\left[Y^{0,0}{=}1\right]$$

A and E have equal status and could also be considered a combined treatment AE, exchangeability for both is needed additive scale (above): ">" superadditive and "<" subadditive; multiplicative scale: ">" super- and "<" submultiplicative difference to effect modification: if E is randomly assigned methods coincide, but V can not be intervened on as E can monotonicity effect is either nonnegative or nonpositive  $\forall i$  sufficient component-cause framework pedagogic model response types for binary A: helped, immune, hurt, doomed; for binary A and E: 16 types (minimal) sufficient causes:

- (minimal)  $U_1$  together with A=1 ensure Y=1
- (minimal)  $U_2$  together with A=0 ensure Y=1

sufficient cause interaction: A and E appear together in a minimal sufficient cause

NPSEM nonparamentric structural equation model

$$V_m = f_m(pa_m, \epsilon_m)$$

counterfactuals are obtained recursively, e.g.  $V_3^{v_1} = V_3^{v_1,V_2^{v_1}}$  implies any variable can be intervened on aka finest causally interpreted structural tree graph (FCISTG) additional assumption  $\cap$  FCISTG  $\Rightarrow$  causal Markov condition:

- independent errors (NPSEM-IE): all  $\epsilon_m$  mutually independent
- fully randomized (FFRCISTG):  $V_m^{\bar{v}_{m-1}} \perp \!\!\! \perp V_j^{\bar{v}_{j-1}}$  if  $\bar{v}_{j-1}$  subvector of  $\bar{v}_{m-1}$

NPSEM-IE  $\Rightarrow$  FFRCISTG (assume DAGs represent latter) NPSEM-IE assume crossworld independencies  $\rightarrow$  unverifiable

Causal DAG draw assumptions before conclusions rules: arrow means direct causal effect for at least one i, absence means sharp null holds, all common causes are on the graph neglects: direction of cause (harmful/protective), interactions convention: time flows from left to right

**causal Markov assumption:** any variable (v) | its direct causes  $(pa_j) \perp \!\!\! \perp$  its non-descendants  $(\neg v_j) \Leftrightarrow$  Markov factorization

$$f(v) = \prod_{j=1}^{M} f(v_j | pa_j)$$

d-separation (d for directional): a pathway in a DAG is ...

- blocked if collider or conditioned on non-collider
- opened if conditioned on collider or descendent of collider 2 variables are d-separated if all connecting paths are blocked under causal Markov: d-separation ⇒ independence under faithfulness: independence ⇒ d-separation faithfulness: effects don't cancel out perfectly discovery: process of learning the causal structure; requires faithfulness, but even with it is often impossible

Noncausal DAGs (Hernán and Robins, 2023)  $Y^a$  has to be well-defined (identifiability), what about  $Y^l$  (if  $L \to Y$ )? if  $Y^l$  is not well-defined, but  $L \to Y$ , then the graph is not causal statistical interpretation: only  $A \to Y$  is causal, the rest simply encodes conditional independencies, but why should a DAG corresponding to the study variables even exist then? hidden factor: L is only a surrogate for H, with  $Y^h$  well-defined, however, L being a surrogate can introduce bias pragmatic approach: "cause" as a primary concept which does not need explanation in terms of well-defined interventions (approach is in need of mathematical theory)

**SWIGs** single world intervention graphs counterfactual graphic approach: A turns into A|a, the left (right) side inherits incoming (outgoing) arrows (intervention with A=a); all outcomes of A get a superscript a, e.g.  $Y^a$ ; more than one intervention possible, dynamic strategies require additional arrows from L to a

A and  $Y^a$  are d-separated for  $L \to Y^a \perp \!\!\! \perp A | L$  (for FFRCISTG)

**Confounding** bias due to common cause of A & Y not in L randomization prevents confounding

backdoor path: noncausal path A to Y with arrow into A backdoor criterion: all backdoor paths are blocked by L & no descendants of A in  $L \Rightarrow$  conditional exchangeability  $Y^a \perp \!\!\!\perp A | L \Rightarrow L$  fulfills backdoor criterion if faithful (FFRCISTG) confounders in observational studies: occupational factors (healthy worker bias), clinical decisions (confounding by indication/channeling), lifestyle, genetic factors (population stratification), social factors, environmental exposures given a DAG, confounding is an absolute, confounder is relative surrogate confounders in L may reduce confounding bias negative outcome controls: if A and Y share a common cause U: measure effect for  $Y_0$  (before treatment) and  $Y_1$  (after), subtract (assumption of additive equi-confounding) front door criterion using the full mediator M:  $\Pr[Y^a = 1] = \sum_{m} \Pr[M = m | A = a] \sum_{n'} \Pr[Y = 1 | M = m, A = a'] \Pr[A = a']$ 

**Selection Bias** bias due to common effect of A & Y in L = conditioning on collider (can't be fixed by randomization) **examples:** informative censoring, nonresponse bias, healthy worker bias, volunteer bias; often M-bias  $(A \leftarrow U_1 \rightarrow L \leftarrow U_2 \rightarrow Y)$  **solution:** target  $Y^{A,C}$ , AC fulfills identifiability conditions, if competing events, interventions may not be well-defined **multiplicative survival model:**  $\Pr[Y=0|E=e,A=a]=g(e)h(a) \rightarrow$  no interaction between E and A on the multiplicative scale; if Y=0 is conditionally independent, then Y=1 can't be as  $\Pr[Y=1|E=e,A=a]=1-g(e)h(a) \rightarrow$  conditioning on a collider could be unbiased if restricted to certain levels (Y=0)

Measurement Bias aka information bias measurements  $X^*$  of variables X can be included in DAG independent errors U if  $f(U_A, U_Y) = f(U_A)f(U_Y)$  nondifferential A: if  $f(U_A|Y) = f(U_A)$ ; Y:  $f(U_Y|A) = f(U_Y)$  mismeasurement  $\to$  bias, if:  $A \to Y$  or dependent or differential reverse causation bias caused by e. g. recall bias: independent but differential A (caused by  $Y \to U_A$ ) misclassified treatment: assignment Z does not determine A

 per-protocol effect: either as-treated (→ confounded) or restricted to protocol adhering individuals (→ selection bias)

exclusion restriction: ensure  $Z \not\to Y$ , e.g. via double-blinding

intention-to-treat effect (→ measurement bias): advantages:
 Z is randomized, preserves null (if exclusion restriction
 holds), = underpowered α-level test of the null (only if
 monotonicity; underpowered may be problematic if treatment
 safety is tested)

sometimes mismeasurement doesn't matter as the measurement itself is of interest (Hernán and Robins, 2023)

Random Variabilty quantify uncertainty due to small n CI: e. g. Wald CI =  $\hat{\theta} \pm 1.96 \times se(\hat{\theta})$ , calibrated if it contains 95% of estimands (>: conservative, <: anticonservative) large sample CI: converge to 95% vs. small-sample: always valid

honest:  $\exists n$  where coverage  $\geq 95\%$ , valid: large-sample & honest inference: either restrict inference to sample (randomizationbased inference) or inference on super-population **super-population:** generally a fiction, but  $\rightarrow$  simple statistical properties (where does the variability of the distribution come from: assumption population is sampled from super-population) conditionality principle: inference should be performed conditional on ancillary statistics (e.g. L-A association) as

$$\mathcal{L}(Y) = f(Y|A, L)f(A|L)f(L)$$

exactly ancillary A, L: f(Y|A, L) depends on parameter of interest, but f(A, L) does not share parameters with f(Y|A, L)approximately ancillary: ... does not share all parameters ... continuity principle: also condition on approximate ancillaries curse of dimensionality: difficult to do conditionality principle

Time-Varying Treatments compare 2 treatments treatment history up to k:  $\bar{A}_k = (A_0, A_1, ..., A_k)$ shorthand: always treated  $\bar{A} = \bar{1}$ , never treated  $\bar{A} = (\bar{0})$ **static strategy:**  $g = [g_0(\bar{a}_{-1}), ..., g_K(\bar{a}_{K-1})]$ dynamic strategy:  $g = [g_0(\bar{l}_0), ..., g_K(\bar{l}_K)]$ stochastic strategy: non-deterministic q optimal strategy is where  $E[Y^g]$  is maximized (if high is good)

Sequential Identifiability sequential versions of exchangibility:  $Y^g \perp \!\!\!\perp A_k | \bar{A}_{k-1} \ \forall g, k = 0, 1, ..., K$  $conditional\ exchangeability:$ 

$$\begin{split} \left(Y^g, L_{k+1}^g\right) \perp \!\!\! \perp A_k | \bar{A}_{k-1} &= g\left(\bar{L}_k\right), \bar{L}^k \ \, \forall g, k = 0, 1, ..., K \\ \text{positivity:} \ \, f_{\bar{A}_{k-1}, \bar{L}_k}(\bar{a}_{k-1}, \bar{l}_k) \neq 0 \ \, \Rightarrow \\ f_{A_k} | \bar{A}_{k-1}, \bar{L}_k(a_k | \bar{a}_{k-1}, \bar{l}_k) > 0 \ \, \forall \left(\bar{a}_{k-1}, \bar{l}_k\right) \end{split}$$

consistency:

$$\begin{split} Y^{\bar{a}} &= Y^{\bar{a}^*} &\text{ if } \bar{a} = \bar{a}^*; & Y^{\bar{a}} &= Y &\text{ if } \bar{A} = \bar{a}; \\ \bar{L}_k^{\bar{a}} &= \bar{L}_k^{\bar{a}^*} &\text{ if } \bar{a}_{k-1} = \bar{a}_{k-1}^*; & \bar{L}_k^{\bar{a}} = \bar{L}_k &\text{ if } \bar{A}_{k-1} = \bar{a}_{k-1} \end{split}$$

generalized backdoor criterion (static strategy): all backdoors into  $A_k$  (except through future treatment) are blocked  $\forall k$ static sequential exchangeability for  $Y^{\bar{a}}$  (weaker version)

$$Y^{\bar{a}} \perp \!\!\!\perp A_k | \bar{A}_{k-1}, \bar{L}_k \quad \text{for } k = 0, 1, ..., K$$

sufficient to identify mean counterfactual outcome for static strategies and can be checked on SWIGS via d-separation time-varying confounding  $E[Y^{\bar{a}}|L_0] \neq E[Y|A=\bar{a},L_0]$ 

**Treatment-Confounder Feedback**  $A_0 \rightarrow L_1 \rightarrow A_1$ : an unmeasured U influencing  $L_1$  and Y turns  $L_1$  into a collider; traditional adjustment (e.g. stratification) biased: use g-methods **g-null test** sequential exchangeability & sharp null true  $\Rightarrow$  $Y^g = Y \forall g \Rightarrow Y \perp \perp A_0 \mid L_0 \& Y \perp \perp A_1 \mid A_0, L_0, L_1$ ; therefore: if last two independences don't hold, one assumption is violated **g-null theorem:**  $E[Y^g] = E[Y]$ , if the two independences hold (⇒ sharp null: only if strong faithfulness (no effect cancelling))

Causal Mediation (Hernán and Robins, 2023)

 $A \longrightarrow M \longrightarrow Y$  seen as longitudinal with  $k_0$ : A and  $k_1$ : M **decompose**  $E[Y^{a=1}] - E[Y^{a=0}]$  into cross-world quantities

• pure (aka natural) direct effect (upper path)

$$\mathbf{E}\left[Y^{a=1,M^{a=0}}\right] - \mathbf{E}\left[Y^{a=0,M^{a=0}}\right]$$

• total (aka natural) indirect effect (lower path) 
$$\mathbf{E}\left[Y^{a=1,M^{a=1}}\right] - \mathbf{E}\left[Y^{a=1,M^{a=0}}\right]$$

mediation formula under NPSEM-IE (requires  $Y^{a=1,m}$   $\perp$  $M^{a=0}$  cross-world independence)

$$E[Y^{a=1,M^{a=0}}] = \sum_{m} E[Y|A=1, M=m] Pr[M=m|A=0]$$

 ${\bf interventional\ interpretation\ advocating\ NPSEM-IE\ assum-}$ 

ing: 
$$A \xrightarrow{\longrightarrow} \stackrel{N}{\longrightarrow} \stackrel{M}{\longrightarrow} Y$$
 (thick arrows are deterministic) no controlled direct effects: no  $N \to Y$  and no  $O \to M$  FFRCISTG point of view: intervention on  $N$  and  $O$  separately if decomposable (can be verified in a randomized trial), g-formula for  $N$  and  $O$  reduces to mediation formula for  $A$ 

## 3 Models

Modeling data are a sample from the target population

 $\begin{array}{lll} \textit{estimand:} & \text{quantity of interest,} & \text{e. g. } \mathbf{E}\left[Y|A=a\right] \\ \textit{estimator:} & \text{function to use,} & \text{e. g. } \widehat{\mathbf{E}}\left[Y|A=a\right] \\ \textit{estimate:} & \text{apply function to data,} & \text{e. g. } 4.1 \\ \end{array}$ 

model: a priori restriction of joint distribution/dose-response curve; assumption: no model misspecification (usually wrong) non-parametric estimator: no restriction (saturated model) = Fisher consistent estimator (entire population data → true value) parsimonious model: few parameters estimate many quantities bias-variance trade-off:

wiggliness  $\uparrow \rightarrow$  misspecification bias  $\downarrow$ , CI width  $\uparrow$ 

Super Learning (van der Laan et al., 2007, 2011) oracle selector: select best estimator of set of learners  $Z_i$  discrete super learner: select algorithm with smallest cross-validated error (converges to oracle for large sample size) super learner: improves asymptotically on discrete version  $\operatorname{logit}(Y=1|Z) = \sum_i \alpha_i Z_i$ , with  $0 < \alpha_i < 1$  and  $\sum \alpha_i = 1$  weights  $\alpha_i$  are determined inside the cross-validation; for the prediction,  $Z_i$  trained on the full data set are used can be cross-validated itself to check for overfitting (unlikely)

Marginal Structural Models association is causation in the IP weighted pseudo-population

associational model  ${\rm E}\left[Y|A\right]={\rm causal\ model\ E}\left[Y^a\right]$  step 1: estimate/model  $f\left[A|L\right]$  (and  $f\left[A\right]$ )  $\to$  get  $(S)W^A$  step 2: estimate regression parameters for pseudo-population **effect modification** variables V can be included (e. g.  $\beta_0+\beta_1a+\beta_2Va+\beta_3V$ ; technically not marginal anymore),  $SW^A(V)=\frac{f\left[A|V\right]}{f\left[A|L\right]}$  more efficient than  $SW^A$ 

#### 3.1 Traditional Methods

**Stratification** calculate risk for each stratum of L only feasible if enough data per stratum

**Outcome Regression** often assume no effect modification  $\mathrm{E}\left[Y^{a,c=0}|L\right] = \beta_0 + \beta_1 a + \beta_2 a L + \beta_3 L = \mathrm{E}\left[Y|A,C=0,L\right]$  faux marginal structural model as no IP weighting/ $SW^A(L) = 1$  for ATE only  $\beta_1,\beta_2$  of interest, the rest are nuisance parameters

**Propensity Score Methods**  $Pr[A = 1|L] =: \pi(L)$ 

 $\Rightarrow A \perp \!\!\!\perp L | \pi(L)$  (definition of a balancing score); can be modelled

- stratification: create strata with similar  $\pi(L)$  (e.g. deciles), but the average  $\pi(L)$  might still be different in some strata
- standardization: use  $\pi(L)$  instead of L to standardize
- matching: find close ( $\rightarrow$  bias-variance trade-off) values of  $\pi(L)$ , positivity issues arise often

propensity models don't need to predict well, just ensure exchangeability (good prediction leads to positivity problems)

Instrumental Variable Estimation L unmeasured surrogate/proxy instruments can be used

#### instrumental conditions:

- 2. exclusion restriction: Z affects Y at most through A
  - (a) population level:  $E[Y^{z,a}] = E[Y^{z',a}]$  (sometimes enough)
  - (b) individual level:  $Y_i^{z,a} = Y_i^{z',a} = Y_i^{a}$
- 3. exchangeability: Z and Y have no shared causes
  - (a) marginal:  $Y^{a,z} \perp \!\!\! \perp Z$  (typically enough)
  - (b) joint:  $\{Y^{z,a}; a \in [0,1], z \in [0,1]\} \perp \!\!\! \perp Z$
- 4. (not needed for an instrument, just the IV estimand below)
  - (a) effect homogeneity: (i) constant effect  $A \to Y \ \forall i$  (ii) constant average effect  $A \to Y \ \forall A$  (iii) no additive effect modifiers (iv) additive Z-A association is constant across L
  - (b) monotonicity:  $A^{z=1} \ge A^{z=0} \ \forall i$  (more credible than 4a)

common instruments: (physician's) general preference, access to/price of A, genetic factors (Mendelian randomization) bounds: binary outcome ATE [-1,1] (width 2)  $\stackrel{data}{\rightarrow}$  (width 1) natural bounds need 2a,3a (width Pr [A=1|Z=0] + Pr [A=0|Z=1]) sharp bounds require 2a,3b (narrower than natural bounds) IV estimand ATE: intention-to-treat  $\div$  measure of compliance (1,2b,3a,4a): ATE; (1,2b,3a,4b): ATE in compliers binary Z:  $\frac{E[Y|Z=1]-E[Y|Z=0]}{E[A|Z=1]-E[A|Z=0]}$ , continuous Z:  $\frac{Cov(Y,Z)}{Cov(A,Z)}$ ; can be calculated as two-stage-least-squares estimator: 1. E[A|Z] 2.  $E[Y|Z] = \beta_0 + \beta_1 \hat{E}[A|Z]$  3.  $\hat{\beta}_1$  is IV estimate disadvantages: often leads to wide CI, small violations of conditions can lead to large biases

**regression discontinuity design:** if threshold in L exists which determines A perfectly + assumption of continuity in  $L \to \text{jump}$  in Y at threshold is the causal effect (if no effect modification by L); a fuzzy variant also exists (Hernán and Robins, 2023)

Causal Survival Analysis time-to-event data additional censoring due to administrative end of follow-up competing events (often death): censoring (assume population with death abolished) or not (after death, chance of event is zero, but what is the effect of A?)  $\rightarrow$  create composite event survival quantities k is a time point, T is time of event

- survival at k:  $Pr[T > k] =: Pr[D_k = 0]$
- risk at k:  $1 Pr[T > k] = Pr[T \le k] = Pr[D_k = 1]$
- hazard at k:  $\Pr[T = k|T > k-1] = \Pr[D_k = 1|D_{k-1} = 0]$ , hazard ratio is paradoxical due to in-built selection bias

modeling: some options

- Kaplan-Meier aka product limit formula (nonparametric):  $\Pr\left[D_k=0\right] = \prod_{m=1}^k \Pr\left[D_m=0|D_{m-1}=0\right]$
- parametric e.g. log hazards model:
  - use IP weigths  $SW^A$  in structural marginal model logit  $\Pr\left[D_{k+1}^{a,\bar{c}=\bar{0}}=0|D_k^{a,\bar{c}=\bar{0}}=0\right]=\beta_{0,k}+\beta_1a+\beta_2ak$
  - standardize ( $\prod_k 1$ -) parametric hazards model  $\Pr[D_{k+1} = 1 | D_k = 0, C_k = 0, L, A]$  weighting across L

- structural nested cumulative failure time model (CFT):  $\frac{\Pr[D_k^a=1|L,A]}{\Pr[D_k^a=0=1|L,A]}=\exp\left[\gamma_k(L,A;\psi)\right]$  (log-linear has no upper  $\lim_{\to} 1 \to \operatorname{rare failure} \uparrow$ ; if  $\downarrow$ , use a survival model (CST)), use g-estimation like with AFT
- ullet accelerated failure time model (AFT) with g-estimation:  $T_i^a/T_i^{a=0} = \exp(-\psi_1 a - \psi_2 a L_i)$ , exchangeability for C is guaranteed via artificial censoring (include only individuals who would not have been censored either way)

time-varying two options based on g-methods as examples standardization (plug-in estimate): risk is  $\Pr\left[D_{k+1}^{\bar{a},\bar{c}=\bar{0}}=1\right]=\sum_{\bar{l}_k}\sum_{j=0}^k\Pr\left[D_{j+1}=0|\bar{A}_j=\bar{a}_j,\bar{L}_j=\bar{l}_j,\bar{D}_j=0\right]\times$ 

$$\sum_{\bar{l}_k} \sum_{j=0}^k \Pr \left[ D_{j+1} = 0 | \bar{A}_j = \bar{a}_j, \bar{L}_j = \bar{l}_j, \bar{D}_j = 0 \right] \rangle$$

$$\prod_{s=0}^{j} \left\{ \Pr \left[ D_{s} = 0 | \bar{A}_{s-1} = \bar{a}_{s-1}, \bar{L}_{s-1} = \bar{l}_{s-1}, \bar{D}_{s-1} = 0 \right] \times f \left( l_{s} | \bar{a}_{s-1}, \bar{l}_{s-1}, D_{s} = 0 \right) \right\}$$

IP weighting: fit a pooled logistic hazard model with timevarying weights  $W_k^{\bar{A}} = \prod_{m=0}^k \frac{1}{f(A_m | \bar{A}_{m-1}, \bar{I}_{\ell m})}$ 

#### 3.2G-Methods

 ${f G-Methods}$  generalized treatment contrasts: adjust for L

- $\bullet \ \ standardization:$  two types of g-formula
- IP weighting: (in theory) also g-formula
- g-estimation: not needed unless longitudinal

standardization and IP weighting are equivalent, but if modeled, different "no misspecification" assumptions: outcome model (standardization), treatment model (IP weighting) big g-formula not all methods use (sequential) exchangeability

- problem: DAG is known, but unmeasured variables exist
- solution: include un- & measured variables in big g-formula → derive alternative effect identification methods using only d-separation (e.g. front door formula)

it can always be determined, if the DAG allows for identification with the big g-formula (Hernán and Robins, 2023)

**censoring:** measure joint effect of A and C with  $E[Y^{a,c=0}]$  $standardization \ \mathbf{E}\left[Y|A=a\right]=\int \mathbf{E}\left[Y|L=l,A=a,C=0\right]dF_{L}\left[l\right]$ 

IP weights 
$$W^{A,C} = W^A \times W^C$$
 (uses  $n$ ) of  $SW^{A,C} = SW^A \times SW^C$  (uses  $n^{c=0}$ )

g-estimation only adjusts for confounding  $\rightarrow$  use IP weights

time-varying censoring  $\bar{C}$ : monotonic type of missing data

standardization: 
$$\int f(y|\bar{a},\bar{c}=\bar{0},\bar{l}) \prod_{k=0}^{K} dF\left(l_{k}|\bar{a}_{k-1},c_{k-1}=0,\bar{l}_{k-1}\right)$$

IP weighting

$$SW^{\bar{C}} = \prod_{k=1}^{K+1} \frac{1 \cdot \Pr\left(C_k = 0 | \bar{A}_{k-1}, C_{k-1} = 0\right)}{\Pr\left(C_k = 0 | \bar{A}_{k-1}, C_{k-1} = 0, \bar{L}_k\right)}$$

Standardization plug-in (parametric if so) g-formula

$$\mathbf{E}\left[Y^{a}\right] = \underbrace{\mathbf{E}\left[\mathbf{E}\left[Y|A = a, L = l\right]\right]}_{\text{conditional expectation}} \underbrace{\int \mathbf{E}\left[Y|A = a, L = l\right] f_{L}\left[l\right] dl}_{\text{conditional expectation}}$$

weighted average of stratum-specific risks; unknowns can be estimated non-parametrically or modeled

no need to estimate  $f_L[l]$ /integrate as empirical distribution can be used: estimate outcome model  $\rightarrow$  predict counterfactuals on whole dataset  $\rightarrow$  average the results ( $\rightarrow$  CI by bootstrapping) for discrete  $L \to [Y|A=a]$  is  $\sum_l \to [Y|A=a, L=l] \Pr[L=l]$ 

time-varying standardize over all possible  $\bar{l}$ -histories simulates joint distribution of counterfactuals  $(Y^{\bar{a}}, \bar{L}^{\bar{a}})$  for  $\bar{a}$ joint density estimator (jde)

$$\text{discrete: } \mathbf{E}\left[Y^{\bar{a}}\right] = \sum_{\bar{l}} \mathbf{E}\left[Y|\bar{A} = \bar{a}, \bar{L} = \bar{l}\right] \prod_{k=0}^{K} f\left(l_{k}|\bar{a}_{k-1}, \bar{l}_{k-1}\right)$$

continuous: 
$$\int f(y|\bar{a},\bar{l}) \prod_{k=0}^K f\left(l_k|\bar{a}_{k-1},\bar{l}_{k-1}\right) dl$$

for stochastic strategies multiply with  $\prod_{k=0}^{K} f^{int}\left(a_k | \bar{a}_{k-1}, \bar{l}_k\right)$ 

estimation (Young et al., 2011; Schomaker et al., 2019)

- 1. model  $f(l_k|\bar{a}_{k-1},\bar{l}_{k-1})$  and  $E[Y|\bar{A}=\bar{a},\bar{L}=\bar{l}]$
- 2. simulate data forward in time: at k = 0: use empirical distribution of  $L_0$  (observed data) at k > 0: set  $\bar{A} = \bar{a}$ , draw from models estimated in 1.
- 3. calculate mean of  $\hat{Y}_{K,i}^{\bar{a}}$  (bootstrap for CI)

iterated conditional expectation (ice)

$$\mathbf{E}\left[Y_{T}^{\bar{a}}\right] = \mathbf{E}\left[\mathbf{E}\left[\mathbf{E}\left[...\mathbf{E}\left[Y_{T}|\bar{A}_{T-1}{=}\bar{a}_{T-1},\bar{L}_{T}\right]...|\bar{A}_{0}{=}a_{0},L_{1}\right]|L_{0}\right]\right]$$

estimation (Schomaker et al., 2019)

- 1. model inside out:  $Q_T = \mathbb{E}\left[Y_T | \bar{A}_{T-1}, \bar{L}_T\right]$  to  $Q_0 = \mathbb{E}\left[Q_1 | \bar{L}_0\right]$ predict  $Q_t$  with  $\bar{A} = \bar{a}$  in each step
- 2. calculate mean of  $\hat{Q}_{0,i}^{\bar{a}}$  (bootstrap for CI)

g-null paradox even if the sharp null holds, model misspecification can lead to it being falsely rejected

LIE: law of iterated expectation

$$\mathbf{E}\left[Y^{a}\right] = \mathbf{E}\left[\frac{I(A=a)Y}{f\left[A|L\right]}\right]; W^{A} = \frac{1}{f\left[A|L\right]}; SW^{A} = \frac{f(A)}{f\left[A|L\right]}$$

unknowns can be estimated non-parametrically or modeled **pseudo-population:** everyone is treated & untreated  $(L \not\rightarrow A)$ FRCISTG (fully randomized causally interpreted structured graph): probability tree for  $L \to A \to Y$ , can be used to calculate/visualize simulation of values for A

for discrete A, L: f[a|l] = Pr[A = a, L = l]

estimators: Horvitz-Thompson; Hajek (modified version) stabilized weights  $SW^A$  should have an average of 1 (check!)

 $\rightarrow$  pseudo-population same size  $\rightarrow$  (if non-saturated) CI width  $\downarrow$ 

$$W^{\bar{A}} = \prod_{k=0}^{K} \frac{1}{f\left(A_{k}|\bar{A}_{k-1},\bar{L}_{k}\right)}; \quad SW^{\bar{A}} = \prod_{k=0}^{K} \frac{f\left(A_{k}|\bar{A}_{k-1}\right)}{f\left(A_{k}|\bar{A}_{k-1},\bar{L}_{k}\right)}$$

G-Estimation (additive) structural nested models

logit Pr 
$$\left[A = 1 | H(\psi^{\dagger}), L\right] = \alpha_0 + \alpha_1 H(\psi^{\dagger}) + \alpha_2 L$$
  
 $H(\psi^{\dagger}) = Y - \psi_{\dagger} A$ 

find  $\psi^{\dagger}$  which renders  $\alpha_1 = 0$ ; 95 %-CI: all  $\psi^{\dagger}$  for which p > 0.05closed-form solution for linear models

**derivation:**  $H(\psi^{\dagger}) = Y^{a=0}$ 

logit Pr 
$$[A = 1|Y^{a=0}, L] = \alpha_0 + \alpha_1 Y^{a=0} + \alpha_2 L$$

 $Y^{a=0}$  unknown, but because of exchangeability  $\alpha_1$  should be zero

$$Y^{a=0} = Y^a - \psi_1 a$$

equivalent to  $Y^{a=0} = Y^{a=1} - \psi_1$ , but using no counterfactuals structural nested mean model

$$\begin{array}{ll} \text{additive:} & \mathrm{E}\left[Y^a-Y^{a=0}|A=a,L\right] & =\beta_1 a\left(+\beta_2 aL\right) \\ \\ \text{multiplicative:} & \log\left(\frac{\mathrm{E}\left[Y^a|A=a,L\right]}{\mathrm{E}\left[Y^{a=0}|A=a,L\right]}\right) & =\beta_1 a\left(+\beta_2 aL\right) \end{array}$$

multiplicative is preferred if Y always positive, but does not extend to longitudinal case

semi-parametric: agnostic about  $\beta_0$  and effect of  $L \to \text{robust} \uparrow$ no time-varying: no nesting; model equals marginal structural models with missing  $\beta_0, \beta_3$  (unspecified "no treatment")

sensitivity analysis: unmeasured confounding  $(\alpha_1 \neq 0)$  can be examined: do procedure for different values of  $\alpha_1 \to \text{plot } \alpha_1 \text{ vs.}$  $\psi^{\dagger} \rightarrow \text{how sensitive is estimate to unmeasured confounding?}$ **effect modification:** add V in both g-estimation equations doubly robust estimators exist

time-varying nested equations: for each time kstrutural nested mean models separate effect of each  $a_k$  $\mathbb{E}\left[Y^{\bar{a}_{k-1},a_k,\underline{0}_{k+1}}-Y^{\bar{a}_{k-1},\underline{0}_{k+1}}|\bar{L}^{\bar{a}_{k-1}}=\bar{l}_k,\bar{A}_{k-1}=\bar{a}_{k-1}\right]=$ 

calculations

$$H_k\left(\psi^{\dagger}\right) = Y - \sum_{j=k}^{K} A_j \gamma_j \left(\bar{A}_{j-1}, \bar{L}_j, \psi^{\dagger}\right)$$

 $a_k \gamma_k \left( \bar{a}_{k-1}, \bar{l}_k, \beta \right)$ 

function  $\gamma_j$  can be, e.g. constant  $(\psi_1)$ , time-varying only  $(\psi_1 +$  $\psi_2 k$ ), or dependent on treatment/covariate history

$$\operatorname{logit} \operatorname{Pr} \left[ A_k = 1 | H_k \left( \psi^{\dagger} \right), \bar{L}_k, \bar{A}_{k-1} \right] =$$

$$\alpha_0 + \alpha_1 H_k \left( \psi^{\dagger} \right) + \alpha_2 w_k \left( \bar{L}_k, \bar{A}_{k-1} \right)$$

find  $\alpha_1$  that is closest to zero

a closed form estimator exists for the linear case

#### 3.3 Doubly Robust Methods

Double-Robustness (Hernán and Robins, 2023) g-formula: either treatment model f(L) or outcome model b(L)or appropriately combine both: "two chances to get it right" all doubly robust estimators

- involve a correction of outcome  $\hat{b}(L)$  using the treatment  $\hat{f}(L)$
- have a bias depending on a product of the errors  $\frac{1}{\pi(l)} \frac{1}{\hat{\pi}(l)}$ and  $b(l) - \hat{b}(l)$  known as second order bias

time-varying: multiple robustness for k = 0, 1, ...KK+2 robustness: consistent, if  $\hat{f}_0$  to  $\hat{f}_l$  and  $\hat{b}_{l+1}$  to  $\hat{b}_K$  are  $2^{K+1}$  robustness: consistent, if for each k, either  $\hat{f}_k$  or  $\hat{b}_k$  are

#### Machine Learning L is high-dimensional

one could use lasso or ML for IP weighting/standardization but: ML does not guarantee elimination of confounding and has largely unknown statistical properties: how to get CI? sample splitting: train estimators on training sample  $T_r$ , use resulting estimators for doubly robust method on estimation sample (CIs on estimation sample are valid, but n halved) cross-fitting: do again the other way round, average the two estimates, get CI via bootstrapping [alternatively: split into Msamples, use one sample for estimation and M-1 for training  $\rightarrow$ improved finite sample behavior (Hernán and Robins, 2023)] **asymptotic behavior** for valid (Wald) CI we need:

- a bias much smaller than  $c \cdot 1/\sqrt{n}$ , which is how the se typically scales (use doubly robust methods for small bias)
- asymptotic normality (for Wald CI)
- for a doubly robust estimator  $\psi_{dr}$ , we need sample splitting, otherwise  $\hat{b}(l)$  and  $\hat{f}(l)$  are correlated with  $\psi_{dr}$ if  $\hat{b}(l)$  and  $\hat{f}(l)$  are consistent and  $E[\hat{\psi} - \psi | T_r]/se(\hat{\psi})$  converges to  $0 \to \hat{\psi}$  with sample splitting is asymptotically normal and unbiased → CI is calibrated (Hernán and Robins, 2023) problems: unclear choice of algorithm, is bias small enough?

Advantages (van der Laan et al., 2011) **consistent** if either  $\bar{Q}_0$  or  $g_n$  are consistent (doubly robust):  $\forall \epsilon > 0, P \in \mathcal{M} : \Pr_P \left[ |\hat{\theta}_n - \theta(P)| > \epsilon \right] \to 0 \text{ as } n \to \infty$ 

collaboratively doubly robust:  $g_n$  only needs predictors of Y, as it does not try to fit  $g_0$  well, but improve the fit of  $\bar{Q}_n^*$ asymptotic unbiasedness if either  $\bar{Q}_0$  or  $g_0$  are consistent, super learning makes  $\bar{Q}_0$  and  $g_n$  max. asymptotically unbiased asymptotic efficiency if both  $\bar{Q}_0$  and  $g_n$  are consistent: achieves Cramer-Rao bound of minimum possible asymptotic variance (requires asymptotic unbiasedness) asymptotic linearity if either  $\bar{Q}_0$  or  $g_n$  are consistent: means estimator behaves like empirical mean

- bias converges to zero at rate smaller than  $1/\sqrt{n}$
- for large n estimator is approximately normally distributed

Influence Curve how robust is an estimator? 
$$IC_{T,P_n}(O) = \lim_{\epsilon \to 0} \frac{T\left[(1-\epsilon)\,P_n + \epsilon \delta_O\right] - T(P_n)}{\epsilon}$$

for estimator T and distribution  $P_n$  with  $0 < \epsilon < 1$ can also be rewritten as a directional derivative at  $P_n$ 

$$IC_{T,P_n} = \frac{d}{d\epsilon} T \left[ (1 - \epsilon) P_n + \epsilon \delta_O \right] = \frac{d}{dP_n} T \left( \delta_O - P_n \right)$$

in direction  $(\delta_O - P_n)$ , where  $P_n$  empirical probability measure that puts mass 1/n on  $O_i$  (Hampel, 1974)

special cases (van der Laan et al., 2011)

- $\overline{IC}(P_0) = 0$  and  $Var(IC(P_0))$  asymptotic variance of the standard estimator  $\sqrt{n}(\psi_n - \psi_0)$ ,  $\rightarrow Var(\hat{\Psi}(P_n)) = \frac{Var_{IC}}{n}$
- efficient IC: an estimator is asymptotically efficient  $\Leftrightarrow$  its influence curve is the efficient influence curve  $IC(O) = D^*(O)$

Delta Method (Zepeda-Tello et al., 2022) estimand is a function of  $\theta$ , i.e.  $\psi := \phi(\theta)$ ,  $Var(\hat{\theta})$  known, but what is  $Var(\hat{\psi})$ ? Taylor's approximation requirements:

- univariate  $\phi$ : differentiable at  $\theta$
- multivariate  $\phi$ :  $\exists \partial_v \phi(\theta)$  (directional derivative)
- functional  $\phi$  (function of functions):  $\exists \partial_v \phi(\theta)$  & coincides with one-sided directional (Hadamard) derivatives ( $\stackrel{*}{=} \nabla \phi(\theta)^T v$ )

first order Taylor (rearranged<sup>†</sup>):  $\phi(\hat{\theta}_n) \stackrel{\sim}{\approx} \phi(\theta) \stackrel{\approx}{+} \partial_{v := \hat{\theta} - \theta} \phi(\theta)$ classical delta method: if  $\{r_n\}_{n=1}^{\infty}$  with  $\lim_{n\to\infty} r_n = \infty$ , where  $r_n(\hat{\theta}_n - \theta)$  converges to  $Z \sim N(0, 1)$  (e.g.  $r_n = \sqrt{n/\sigma^2}$ ), then  $r_n\left(\phi(\hat{\theta}_n) - \phi(\theta)\right) \stackrel{\dagger *}{\approx} \nabla \phi(\theta)^T r_n(\hat{\theta}_n - \theta) \stackrel{d}{\to} \nabla \phi(\theta)^T Z$ 

 $\Rightarrow \operatorname{Var}\left[\phi(\hat{\theta}_n) - \phi(\theta)\right] = \operatorname{Var}\left[\phi(\hat{\theta}_n)\right] \approx \frac{1}{r^2}\operatorname{Var}\left[\nabla\phi(\theta)^TZ\right]$ 

functional delta:  $r_n(\hat{\theta}_n - \theta) \xrightarrow{d} Z \Rightarrow r_n(\phi(\hat{\theta}_n) - \phi(\theta)) \xrightarrow{d} \partial_Z \phi(\theta)$ **influence function:**  $\psi = \phi(\mathbb{P}_X)$  is a functional

estimations rate of change for  $\mathbb{P}_X$  to Q, where  $Q = \mathbb{1}_{\{Y\}}$ 

$$\operatorname{IF}_{\phi,\mathbb{P}_X}(Y) := \partial_{Q-\mathbb{P}_X} \phi(\mathbb{P}_X) = \lim_{h\downarrow 0} \frac{\phi\left((1-h)\mathbb{P}_X + hQ\right) - \phi(\mathbb{P}_X)}{h},$$

interpretation: rate of change if distribution deviates from  $\mathbb{P}_X$  to Q = one observation Y, assigns probability 1 to X taking value Yuse delta:  $\phi(\hat{\mathbb{P}}_X) \approx \phi(\mathbb{P}_X) + \mathrm{IF}_{\phi,\mathbb{P}_X}(Y)$ , if  $(\hat{\theta}_n - \theta) \stackrel{n \to \infty}{\sim} \mathrm{N}(.,.)$   $\hat{\psi}_n - \psi = \phi(\hat{\theta}_n) - \phi(\theta) \stackrel{\mathrm{approx}}{\sim} \mathrm{N}\left(0, \mathrm{Var}[\mathrm{IF}_{\phi,\mathbb{P}_X}(Y)]\right)$ ,

$$\hat{\psi}_{n} - \psi = \phi(\hat{\theta}_{n}) - \phi(\theta) \overset{\text{approx}}{\sim} \text{N}\left(0, \text{Var}[\text{IF}_{\phi, \mathbb{P}_{X}}(Y)]\right)$$

where  $\widehat{\operatorname{Var}}[\operatorname{IF}_{\phi,\mathbb{P}_X}(Y)] = \frac{1}{n} \sum_{i=1}^n \left(\operatorname{IF}_{\phi,\mathbb{P}_X}(X_i)\right)^2$ , which is the classical  $S^2$  estimator since the mean is known (= 0)

#### using the delta method (general case)

- 1. determine asymptotic distribution of  $v := r_n(\hat{\theta}_n \theta)$
- 2. define  $\phi$  and compute Hadamard derivative
- 3. multiply asymptotic distribution with Hadamard derivative, then estimate the variance

### Simple Plug-In Estimator proto-TMLE

1. fit outcome regression with variable  $R = \begin{cases} -W^A & \text{if } A=1 \\ -W^A & \text{if } A=0 \end{cases}$ 2. standardize by averaging

time-varying K + 2 robust estimator (related to TMLE)

- 1. estimate  $\hat{f}(A_m|\bar{A}_{m-1},\bar{L}_m)$  (e.g. logistic model), use it to calculate at each time m:  $\widehat{W}^{\bar{A}_m} = \prod_{k=0}^m \frac{1}{\widehat{f}(A_k|\bar{A}_{k-1},\bar{L}_k)}$  and modified IP weights at m:  $\widehat{W}^{\bar{A}_{m-1},a_m} = \frac{\widehat{W}^{\bar{A}_{m-1}}}{\widehat{f}(a_m|\bar{A}_{m-1},\bar{L}_m)}$
- 2. with  $\widehat{T}_{K+1} := Y$ , recursively for m = K, K-1, ..., 0: (a) fit outcome regression on  $\widehat{T}_{m+1}$  with variable  $\widehat{W}^{\bar{A}_m}$ 
  - (b) calculate  $\widehat{T}_m$  using the outcome model with  $\widehat{W}^{\bar{A}_{m-1,a_m}}$
- 3. calculate standardized mean outcome  $\widehat{\mathbf{E}}[Y^{\bar{a}}] = \mathbf{E}[\widehat{T}_0]$

#### Augmented IPTW (Hernán and Robins, 2023)

$$\hat{\mathbf{E}}\left[Y^a\right] = \frac{1}{n}\sum_{i=1}^n \left[\frac{\mathbbm{1}(A=a)Y}{\hat{f}(A|L)} - \left(\frac{\mathbbm{1}(A=a)}{\hat{f}(A|L)} - 1\right)\hat{b}(a,L)\right]$$

disadvantages: ignores global constraints  $\rightarrow$  often unstable if sparsity, sometimes not well-defined (van der Laan et al., 2011)

Relationship between AIPTW and TMLE for causal effect:  $\hat{\psi}_{1,AIPTW} - \hat{\psi}_{0,AIPTW} = P_n \left[ \hat{b}(1,L) \right] - P_n \left[ \hat{b}(0,L) \right]$ 

$$-P_{n} \left[ \frac{\{\mathbb{1}(A=1) - \mathbb{1}(A=0)\} \left(Y - \hat{b}(A, L)\right)}{\hat{f}(A|L)} \right]^{\dagger}$$

using the IRLS estimate for using the IVLS estimate for  $b(A,L;\beta,\theta) = \phi \left[ m(A,L;\beta) + \theta \left\{ \frac{1(A=1) - 1(A=0)}{\hat{f}(A|L)} \right\} \right] \text{ with canon-}$ ical link  $\phi$  sets the last part<sup>†</sup> to zero (as the score equation for  $\theta$ )

TMLE (van der Laan and Rubin, 2006; van der Laan et al., 2011) targeted maximum likelihood estimation: an ML-based substitution estimator of the g-formula Q

$$O = (W, A, Y) \sim P_0; \quad \mathcal{L}(O) = \Pr(Y|A, W) \Pr(A|W) \Pr(W)$$

target  $\Psi(P_0) = \Psi(\bar{Q}_0, Q_{W,0}) = \psi_0, ATE: \bar{Q}_0 = E_0(Y|A, W)$ 

- first step: outcome model  $\bar{Q}_n^0(A, W)$  estimating  $\bar{Q}_0$  (part of  $P_0$ ) • super learning is often used here, but leads to a biased estimate
- not all of  $P_0$  is estimated, just relevant portion  $\bar{Q}_0 \to \text{efficiency}$

**second step:** update  $\bar{Q}_n^0(A,W)$  to  $\bar{Q}_n^1(A,W)$  using treatment model  $g_n$  estimating  $g_0 = P_0(A|W)$ , e. g. for binary A:

- 1. model  $g_n$ , super learning is a popular choice here, too
- 2. calculate n clever covariates:  $H_n^*(A, W) = \begin{cases} \frac{1}{g_n(1|W)} \\ \frac{-1}{g_n(0|W)} \end{cases}$
- 3. update  $\bar{Q}_n^0$ , by estimating  $\epsilon_n$  with offset logistic regression:  $\operatorname{logit} \bar{Q}_{n}^{1}(A, W) = \operatorname{logit} \bar{Q}_{n}^{0}(A, W) + \epsilon_{n} H_{n}^{*}(A, W)$ (converges after first update), then calculate counterfactuals
- goal: bias reduction, get optimal bias-variance trade-off
- · removes all asymptotic bias, if consistent estimator is used here third step: use empirical distribution for  $Q_{W,0}$  in a substitution estimator, e. g.:  $\psi_n^{TMLE} = \frac{1}{n} \sum_{i=1}^n \left[ \bar{Q}_n^1(1, W_i) - \bar{Q}_n^1(0, W_i) \right]$ advantages: loss-based (does not only solve efficient influence curve estimating equation, but also uses a loss and working model preserving global constraints), well-defined (as a loss-based learner), substition estimator (respects global constraints  $\rightarrow$  more robust to outliers and sparsity)  $\rightarrow$  good finite sample performance closed form inference based on the influence curve, e.g.:

$$IC_n^*(O_i) = \underbrace{\left[\frac{\mathbb{I}(A_i = 1)}{g_n(1, W_i)} - \frac{\mathbb{I}(A_i = 0)}{g_n(0, W_i)}\right] \left[Y - \bar{Q}_n^1(A_i, W_i)\right]}_{b} + \underbrace{\bar{Q}_n^1(1, W_i) - \bar{Q}_n^1(0, W_i) - \psi_{TMLE, n}}^{b}$$

TMLE sets the mean of the IC,  $\overline{IC}_n$ , to zero (b has already mean zero, see third step, MLE sets the sum of a to zero, if  $H_n^*(A, W)$ is chosen correctly  $\rightarrow$  the first part of a is the clever covariate) sample variance is then:  $S^2(IC_n) = \frac{1}{n} \sum_{i=1}^n \left(IC_n(o_i) - \bar{IC}_n\right)^2$  standard error of estimator:  $\sigma_n = \sqrt{\frac{S^2(IC_n)}{n}}$ 95% CI:  $\psi_{TMLE,n} \pm z_{0.975} \frac{\sigma_n}{\sqrt{n}}$ ; p-value:  $2 \left[ 1 - \Phi \left( \left| \frac{\psi_{TMLE,n}}{\sigma_n/\sqrt{n}} \right| \right) \right]$ 

time-varying LTMLE (Schomaker et al., 2019; van der Laan and Gruber, 2012) longitudinal TMLE: based on ice g-formula for t = T, ..., 1:

- 1. model  $\widehat{\mathbf{E}}(Y_t|\bar{A}_{t-1},\bar{L}_t)$  (for individuals observed at t-1)
- 2. plug in  $\bar{A}_{t-1} = \bar{d}_{t-1}$ ; use regression from step 1 to predict outcome at time t, i. e.  $\bar{Y}_t^{d_t}$
- 3. update estimate with  $\bar{Y}_{t,\text{new}}^{\bar{d}_t} = \text{offset}(\bar{Y}_t^{\bar{d}_t}) + \epsilon \hat{H}(\bar{A}, \bar{C}, \bar{L})_{t-1}$ : update  $\bar{Y}_t^{\bar{d}_t}$  (or regress offset $(\bar{Y}_t^{\bar{d}_t}) + \epsilon 1$  with weights  $\hat{H}(\bar{A}, \bar{C}, \bar{L})_{t-1}$ ), with clever covariate (without censoring):  $\hat{H}(\bar{A}, \bar{L})_{t-1} = \prod_{s=0}^{t-1} \frac{\mathbb{1}(\bar{A}_s = \bar{d}_s)}{\widehat{\Pr}(A_s = d_s | \bar{A}_{s-1} = \bar{d}_{s-1}, \bar{L}_s = \bar{l}_s)}$
- 4.  $\hat{\psi}_T = \text{mean of } \bar{Y}_1^{\bar{d}_1}, \text{ get CI using influence curve}$ result is a K + 2 multiply robust estimator (Díaz et al., 2021)

#### targeted minimum loss-based estimation

target parameter  $\Psi: \mathcal{M} \to \mathbb{R}$ , with  $\mathcal{M}$  the statistical model used

- 1. compute  $\Psi$ 's pathwise derivative at P and its corresponding canonical gradient  $D^*(P)$  (efficient influence curve)
- 2. define a loss L() s.t.  $P \to E_0L(P)$  is minimized at true  $P_0$
- 3. for a P in model  $\mathcal{M}$  define a parametric working model  $\{P(\epsilon):\epsilon\}$  s. t.  $P(\epsilon=0)=P$  and a "score"  $\frac{d}{d\epsilon}L(P(\epsilon))$  s. t. it (or linear combination of its components) equals  $D^*(P)$  at P
- 4. compute  $\epsilon_n^0 = \arg\min_{\epsilon} \sum_{i=1}^n L(P_n^0(\epsilon))(O_i)$ , with initial estimate  $P_n^0$ , then first iteration  $P_n^1 = P_n^0(\epsilon_n^0)$ , repeat until  $\epsilon_n^k = 0$
- 5. get TMLE estimate  $\psi_0$  by plugging  $P_n^*$  into  $\Psi$  (substitution)
- 6. TMLE solves the efficient influence curve equation

 $\sum_{i=1}^{n} D^{*}(P_{n}^{*})(O_{i}) = 0 \rightarrow \text{asymptotic linearity and efficiency}$ can also be carried out for a relevant part Q instead of all of P

LMTP (Díaz et al., 2021) modified treatment policies **problems** for (longitudinal) continuous or multi-valued A:

• fixed value counterfactuals unrealistic

- infinite-dimensional dose-response curve needs parametric assumptions or is not  $n^{1/2}$  consistent
- positivity is often violated

**solution:** longitudinal MTP  $A_t^{\mathrm{dl}} = \mathrm{dl}\left(A_t(\bar{A}_{t-1}^{\mathrm{dl}}), H_t(\bar{A}_{t-1}^{\mathrm{dl}})\right)$ , e.g. threshold  $(\max(c, a_t))$ , shift  $(a_t + \delta \text{ if positivity else } a_t)$ , stochastic (draw from  $F(\mathrm{dl}(A_t, H_t)|H_t)$ ; randomizer  $\perp \!\!\! \perp U, P$ ), shifted propensity score (only for binary A)

identification for a given NPSEM, assumptions:

- positivity if  $(a_t, h_t)$  in supp $\{A_t, H_t\}$  then  $(d(a_t, h_t), h_t)$  too
- sequential randomization:
  - standard  $U_{A,t} \perp \!\!\!\perp \underline{U}_{L,t+1} | H_t$  (for stochastic LMTP)
- strong  $U_{A,t} \perp \!\!\! \perp (\underline{U}_{L,t+1},\underline{U}_{A,t+1})|H_t$  (for other LMTP) iterative process: set  $m_{\tau+1}:=Y$ , for  $t=\tau,...,1$ :  $m_t:(a_t,h_t)\mapsto \mathrm{E}\left[m_{t+1}(A^{\mathrm{d}}_{t+1},H_{t+1})|A_t=a_t,H_t=h_t\right]$  solve  $\theta=\mathrm{E}\left[m_1(A^{\mathrm{d}}_1,L_1)\right]$

optimality limitations: threshold LMTPs can't be  $n^{1/2}$  consistent as parameter not pathwise differentiable, continuous A can only be considered, if  $d(\cdot, h_t)$  piecewise smooth invertible efficient influence curve (assumes  $d \perp P$ ):

$$EIF\left(\mathrm{E}\left[m_{1}(A^{\mathrm{dl}},L_{1})\right]\right)=\phi_{1}(Z)-\theta$$

with  $r_t(a_t, h_t) = \frac{g_t^{\mathrm{d}}(a_t|h_t)}{g_t(a_t|h_t)}$  and  $\phi_t : z \mapsto \sum_{s=t}^{\tau} \left(\prod_{k=t}^s r_k(a_k, h_k)\right)$  $\left\{m_{s+1}(a_{s+1}^{\mathrm{d}}, h_{s+1}) - m_s(a_s, h_s)\right\} + m_t(a_t^{\mathrm{d}}, h_t)$ 

**estimation** use Super Learner for  $\hat{r}_t$  and  $\hat{m}_t$ 

- g-methods: asymptotically linear and  $n^{1/2}$  consistent if models correctly specified, asymptotic distribution generally unknown substitution (standardization):  $\hat{\theta}_{\text{sub}} = \frac{1}{n} \sum_{i=1}^{n} \hat{m}_1(A_{1,i}^{\text{d}}, L_{1,i})$  $IPTW: \hat{\theta}_{\text{iptw}} = \frac{1}{n} \sum_{i=1}^{n} \left( \prod_{t=1}^{\tau} \hat{r}_t(A_{t,i}, H_{t,i}) \right) Y_i$
- TMLE: use sample splitting and cross-fitting with sets  $\mathcal{T}_j$ , TMLE sets cross-validated EIF  $P_n\Big\{\phi_1(.,\tilde{\eta}_j(.))-\hat{\theta}_{\mathrm{tmle}}\Big\}$  to zero  $\tau+1$  multiply robust &  $n^{1/2}$  consistent (if nuisance consistant) step 1: initialize  $\tilde{\eta}=\hat{\eta}$  and  $\tilde{m}_{\tau+1,j(i)}(A_{\tau+1,i}^{\mathrm{d}},H_{\tau+1,i})=Y_i$  step 2: compute  $\tau$  weights  $\omega_{s,i}=\prod_{k=1}^s\hat{\tau}_{k,j(i)}(A_{k,i},H_{k,i})$

step 3: for  $t= au,\ldots,1$ : fit generalized linear tilting model  $\operatorname{link} \tilde{m}^{\epsilon}_t(A_{t,i},H_{t,i})=\epsilon+\operatorname{link} \tilde{m}_{t,j(i)}(A_{t,i},H_{t,i})$ 

with the canonical link and use  $\hat{\epsilon}$  to update  $\tilde{m}_{t,j(i)}^{\hat{\epsilon}}$ 

step 4:  $\hat{\theta}_{\text{tmle}} = \frac{1}{n} \sum_{i=1}^{n} \tilde{m}_{1,j(i)}(A_{1,i}^{\text{d}}, L_{1,i})$ 

•  $SDR: 2^{\tau}$  multiply robust (sequentially double robust) and same rate of  $n^{1/2}$  consistency as TMLE, better finite sample behavior than TMLE but estimate is not guaranteed to be in support  $step \ \theta$ : cross-fit estimates  $\hat{r}_{1,j(i)},...,\hat{r}_{\tau,j(i)}$ 

step 1: 
$$\phi_{\tau+1}(Z_i; \check{\underline{\eta}}_{\tau,j(i)}) = Y_i$$
  
step 2: for  $t = \tau, ..., 1$ :

- compute pseudo-outcome  $\check{Y}_{t+1,i} = \phi_{t+1}(Z_i; \check{\underline{\eta}}_{\tau,j(i)})$
- for j=1,...,J: regress  $\check{Y}_{t+1,i}$  on  $(A_{t,i},H_{t,i})$  only using  $i\in\mathcal{T}_j$ , with  $\check{m}_{t,j}$  output, update  $\underline{\check{\eta}}_{t,j}=(\hat{r}_{t,j},\check{m}_{t,j},...,\hat{r}_{\tau,j},\check{m}_{\tau,j})$  step 3:  $\hat{\theta}_{\mathrm{sdr}}=\frac{1}{n}\sum_{i=1}^{n}\phi_1(Z_i,\check{\eta}_{j(i)})$
- \* estimate density ratio  $r_t$ : duplicate dataset, where duplicates get assigned  $A_t^{\mathrm{d}}$  with indicator  $\Lambda \in \{0,1\}$   $r_t(a_t,h_t) \stackrel{1}{=} \frac{p^{\lambda}(a_t,h_t|\Lambda=1)}{p^{\lambda}(a_t,h_t|\Lambda=0)} \stackrel{2}{=} \frac{P^{\lambda}(\Lambda=1|A_t=a_t,H_t=h_t)}{P^{\lambda}(\Lambda=0|A_t=a_t,H_t=h_t)} \stackrel{3}{=} \frac{u_t^{\lambda}(a_t,h_t)}{1-u_t^{\lambda}(a_t,h_t)}$  with 1 definition of  $r_t$ , 2 Bayes rule, and 3 by definition  $\Rightarrow$  any classification method can be used (e. g. Super Learning), cross-fitting should be used

Methods for continuous A (Kennedy et al., 2017)

doubly robust methods possible for continuous A for parametric effect curves otherwise a  $\sqrt{n}$  consistent estimator can not exist **procedure:** found double robust  $\xi$  using efficient influence curve in  $\mathbb{E}\left\{\xi(Z;\bar{\pi},\bar{\mu})|A=a\right\}=\theta(a)$ , with data Z and nuisance  $\pi,\mu$  step 1: estimate nuisance  $\pi,\mu$  and predict

step 2: construct pseudo-outcome  $\hat{\xi}(Z; \hat{\pi}, \hat{\mu})$  and regress on A (e.g. using local linear kernel regression)

consistent if: either  $\bar{\pi} = \pi$  or  $\bar{\mu} = \mu$ ,  $\theta(a)$  twice continuously differentiable (and two other items are continuous, assumptions on the kernel part and the function class of nuisance) asymptotic normality if at least one nuisance is fast enough TMLE version a clever covariate is given by the authors

## References

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