# A note on the potential outcomes framework in continuous time

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#### ABSTRACT

In this brief note, we consider the target parameters of Ryalen (2024) and compare it with the target parameter given in Rytgaard et al. (2022), corresponding to their marked point process settings. It is shown that the resulting target parameters are the same if and only if the probability of being treated given that you go to the doctor at time t is equal to 1 for Lebesgue-almost all t, provided that the transition hazards for dying are strictly positive for almost all t.

### 1 Introduction

The aim of this note is to clarify potential differences between the target parameters and identification formulas of Helene and Pål. Throughout we consider a simple setting without censoring, without time-varying covariates and without baseline covariates.

### 2 The intervened world

In a hypothetical world where the intervention is implemented all persons are treated until death or t years after the start of treatment, whatever comes first. We could imagine that a pump is inserted under the persons skin which injects the treatment and that this pump cannot be removed or stopped by a general practitioner.

We further assume that there is absolutely no effect on death of visiting the general practitioner in this hypothetical world. Hence, the hypothetical world can be described with a simple two-stage model and stochastic process  $(X^*(s) \in \{0 = \text{treated}, 1 = \text{death}\})_{s \geq 0}$ . The target parameter can be expressed as:

$$P(X^*(t) = 1) = \int_0^t h^*(s)ds,$$

where  $h^*$  is the hazard rate of transitions from state 0 to state 1.

We can as well use an irreversible three state model where death is the only absorbing state and stochastic process  $(X^**(s) \in \{0 = \text{treated}, 1 = \text{has visited Tivoli}, 2 = \text{death}\})_{s \geq 0}$ . Here the irreversible intermediate state is 'has visited Tivoli' which should not change the likelihood of death. Note that since we assume absolutely no effect by visiting a general practitioner we could simply exchange 'Tivoli' with 'visit to a general practitioner' and the mathematical formula are not altered. In this model the basic assumption is

$$P(X^{**}(t) = 2|X^**(s) = 1) = P(X^{**}(t) = 2|X^{**}(s) = 0)$$

$$P(X^{**}(t) = 2) = P(X^{*}(t) = 1.$$

## 3 The observed world

The observed world is described by the four state multi-state model depicted in Figure 1. The model assumes that all persons are treated at time 0 and then allows that some persons visit a general practitioner which leads to stopping the treatment. We allow for at most one visitation time per person that is the treatment can only be stopped at a single date in time. We observe the counting processes  $N_t = (N_t^{01}, N_t^{02}, N_t^{03}, N_t^{13}, N_t^{23})$  on the canonical filtered probability space  $\left(\Omega, \mathcal{F}, (\mathcal{F}_t)_{t\geq 0}, P\right)$ , where  $\mathcal{F}_t = \sigma(N_s \mid s \leq t)$ . This means that we can represent the observed data as  $O = \left(T_{(1)}, D_{(1)}, T_{(2)}\right)$ , where  $T_{(1)}$  is the first event time,  $D_{(1)} \in \{01, 02, 03\}$  is the first event type,  $A(T_1) = \mathbb{1}\{D_1 \neq 02\}$  is the treatment at the first event time, and  $T_{(2)}$  is the second event time, possibly  $\infty$ . We will assume that the distributions of the jump times are continuous and that there are no jumps in common between the counting processes. By a well-known result for marked point processes (Proposition 3.1 of Jacod (1975)), we know there exists functions  $h^{ij}$ , such that the compensators  $\Lambda^{ij}$  of the counting processes  $N^{ij}$  with respect to  $P - \mathcal{F}_t$  are given by

$$\Lambda^{0j}(dt)=\mathbbm{1}\Big\{t\leq T_{(1)}\Big\}h^{0j}(t)dt,\quad j=1,2,3$$
 
$$\Lambda^{i3}(dt)=\mathbbm{1}\Big\{T_{(1)}< t\leq T_{(2)}\Big\}h^{i3}\Big(T_{(1)},t\Big)dt,\quad i=2,3$$
 We let  $S_0(t)=\prod_{s\in(0,t]}\Big(1-\sum_j h^{0j}(s)ds\Big)$  and  $S_1(t\mid d,s)=\prod_{u\in(s,t]}\Big(1-\sum_i h^{i3}(s,u)\mathbbm{1}\{d=i\}du\Big)$  be the survival functions for the first and second event times, respectively. Furthermore, denote by  $P_{0j}(t)=\int_0^t S_{s-}h^{0j}(s)ds$  the probability of having an of type  $j$  at time by time  $t$  and

be the survival functions for the first and second event times, respectively. Furthermore, denote by  $P_{0j}(t) = \int_0^t S_{s-}h^{0j}(s)ds$  the probability of having an of type j at time by time t and  $P_{i3}(t \mid d,s) = \int_s^t S_1(w-\mid d,s)h^{i3}(s,w)dw$  be the probability of having a terminal at time t given that the first event was of type d at time s.

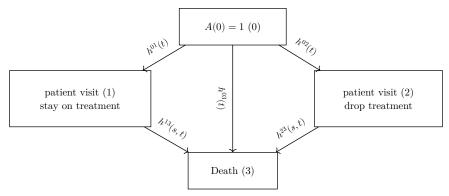


Figure 1: A multi-state model allowing one visitation time for the treatment with the possible treatment values 0/1.

# 4 The potential outcomes framework

To follow along Ryalen (2024), we restrict the observations to the interval  $[0, \tau]$  for  $\tau > 0$ . We first need to define the intervention of interest, defining the counting processes that we would have like to have observed under the intervention. We can intervene on two components of N ( $N^{02}, N^{01}$ ), defining the "interventional" processes as

$$N_t^{g,0} = 0$$
$$N_t^{g,1} = N_t^{01} + N_t^{02}$$

This treatment regime defines that the doctor always treats the patient at the visitation time and does not prevent the patient from visiting the doctor if they drop out of the treatment. This thus dictates that an individual that transitioned from 0 to 2 should instead transition to 1. We define  $T^{a,g}$  as the first time where the observed and the interventional process deviate.

Define also the single "intervention" process

$$N_t^{g^*,0} = N_t^{g,0} = 0$$

where the interventional component is  $N^{02}$ . This dictates that an individual that transitioned from 0 to 2 should not transition to anything at that point. This intuitively thus means that a patient is prevented from visiting the doctor if they drop out of the treatment. The key issue in Ryalen (2024) is that we will not be able to differentiate between target parameters for q and  $q^*$ . The reason is that the likelihood under the intervention only depends on the stopping time  $T^a$  and the problem that the stopping time  $T^a$  is the same under g and  $g^*$ .

To see this, let  $T^{a,g^*}$  be the first time where the observed and the interventional process (according to  $q^*$ ) deviate. We have

$$T^{a,g} = \inf_{t>0} \left\{ N_t^{g,0} \neq N_t^{01} \right\} \wedge \inf_{t>0} \left\{ N_t^{g,1} \neq N_t^{02} \right\} = \inf_{t>0} \left\{ N_t^{g,0} \neq 0 \right\} = \inf_{t>0} \left\{ N_t^{g^*,0} \neq 0 \right\} = T^{a,g^*}$$

Applying Theorem 4.1, we find that the target parameters are the same because the weights  $W_t$  are the same under g and  $g^*$ . Also note that  $\mathbb{1}\{T^a \leq t\} = N^{02}(t)$ .

We now define the target parameter of interest in Ryalen (2024). The outcome of interest is death at time t, i.e.,

$$Y_t = N_t^{13} + N_t^{03} + N_t^{23} = \mathbb{1}\{T_1 \leq t, D_1 = y\} + \mathbb{1}\{T_2 \leq t\}$$

and we want to estimate  $\mathbb{E}_P \big[ \tilde{Y}_t \big]$  where  $\tilde{Y}_t$  denotes the outcome at time t, had the treatment regime (staying on treatment), possibly contrary to fact, been followed.

**Theorem 4.1** (Theorem 1 of Ryalen (2024)): We suppose that there exists a potential outcome process  $\left(\tilde{Y}_{t}\right)_{t\in[0,\tau]}$  such that

- 1. Consistency:  $\tilde{Y}_t \mathbb{1}\{T^A > t\} = Y_t \mathbb{1}\{T^A > t\}$  for all t > 0 P-a.s.
- Consistency. It is for all t > t f of the t > 0 f each.
  Exchangeability: The P − F<sub>t</sub> compensators Λ<sup>01</sup>, Λ<sup>02</sup> are also compensators for G<sub>t</sub> = F<sub>t</sub> ∨ σ(Ỹ<sub>s</sub>, τ ≥ s ≥ 0). Here Ỹ<sub>s</sub> is added at baseline, so that G<sub>0</sub> = σ(Ỹ<sub>s</sub>, τ ≥ s ≥ 0).
  Positivity: W<sub>t</sub> = (1 {T<sup>A</sup>>t} exp(-Λ<sup>02</sup>(t)) = (1 {T(1)≤t,D(1)=a,A(1)=0} exp(-∫<sub>0</sub><sup>t</sup> 1{s≤T(1)}h<sup>a</sup>(s)π<sub>s</sub>(0)ds)<sup>1</sup> is a uniformly integrable martingale or equivalently that R<sup>Pål</sup> given by dR<sup>Pål</sup> = W<sub>τ</sub>dP is a probability measure.

Then the estimand of interest  $\Psi_t^{\text{Ryalen}}: \mathcal{M} \to \mathbb{R}_+$  is identifiable by

$$\Psi_t^{\mathrm{Ryalen}}(P) \coloneqq \mathbb{E}_P \left[ \tilde{Y}_t \right] = \mathbb{E}_P[Y_t W_t] = \mathbb{E}_{R^{\mathrm{Pål}}}[Y_t]$$

From this, we can derive an alternate representation of the target parameter. We have that

<sup>&</sup>lt;sup>1</sup>In the notation of Ryalen (2024),  $\tau^A = T^a$ ,  $\mathbb{N}_t = \mathbb{1}\{T^A \leq t\} = N_t^{02}$  and  $\Lambda_t^{02}$  is the compensator of this process.

$$\begin{split} & \Psi_t^{\text{Ryalen}}(P) = \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(1)} \leq t \right\} Y_t W_t \right] + \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(2)} \leq t \right\} Y_t W_t \right] \\ & = \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(1)} \leq t \right\} Y_t \frac{1 - \mathbb{1} \left\{ T^a > t \right\}}{\exp \left( - \int_0^{T_{(1)}} h^{02}(s) ds \right)} \right] \\ & + \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(2)} \leq t \right\} Y_t \frac{1 - \mathbb{1} \left\{ T^a > t \right\}}{\exp \left( - \int_0^{T_{(1)}} h^{02}(s) ds \right)} \right] \\ & = \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(1)} \leq t, D_{(1)} = 03 \right\} \frac{1}{\exp \left( - \int_0^{T_{(1)}} h^{02}(s) ds \right)} \right] \\ & + \mathbb{E}_P \left[ \mathbb{1} \left\{ T_{(2)} \leq t, D_{(1)} = 01 \right\} \frac{1}{\exp \left( - \int_0^{T_{(1)}} h^{02}(s) ds \right)} \right] \\ & = \int_0^t \frac{1}{\exp \left( - \int_0^t h^{02}(s) ds \right)} P_{03}(dt) \\ & + \int_0^t \frac{1}{\exp \left( - \int_0^t h^{02}(s) ds \right)} P_{13}(t \mid 01, s) P_{01}(ds) \\ & = \int_0^t \exp \left( - \sum_{j \neq 2} \int_0^s h^{0j}(u) du \right) h^{03}(s) ds \\ & + \int_0^t \exp \left( - \sum_{j \neq 2} \int_0^s h^{0j}(u) du \right) P_{13}(t \mid 01, s) h^{01}(s) ds \end{split}$$

## 4.1 The target parameter in Rytgaard et al. (2022)

To discuss Rytgaard et al. (2022), additionally define

$$\begin{split} &\Lambda^a(t) = \big(h^{01}(t) + h^{02}(t)\big)\mathbb{1}\Big\{T_{(1)} \leq t\Big\} \\ &\pi_t(1) = \frac{h^{01}(t)}{h^{01}(t) + h^{02}(t)} \end{split}$$

Here, we can interpret  $\Lambda^a(t)$  as the cumulative intensity of the visitation times (i.e.,  $N_t^a=N_t^{01}+N_t^{02}$ ) and  $\pi_t(1)$  as the probability of being treated given that you go to the doctor at time t. Furthermore, let  $N_t^d=N_t^{03}+N_t^{13}+N_t^{23}$  be the counting process for the event of interest. Then, its compensator is given by

$$\begin{split} \Lambda^d(dt) &= \mathbb{1} \Big\{ t \leq T_{(1)} \Big\} h^{03}(t) dt \\ &+ \mathbb{1} \Big\{ T_{(1)} < t \leq T_{(2)} \Big\} \Big( \mathbb{1} \Big\{ D_{(1)} = 01 \Big\} h^{13} \Big( T_{(1)}, t \Big) + \mathbb{1} \Big\{ D_{(1)} = 02 \Big\} h^{23} \Big( T_{(1)}, t \Big) \Big) dt \end{split}$$

Furthermore, let  $A(t) = \mathbbm{1} \left\{ T_{(1)} > t \right\} + \mathbbm{1} \left\{ T_{(1)} \leq t, D_{(1)} \neq 02 \right\}$  be the treatment process at time t. Notationwise, we also define  $\Delta N(t) = N_t - N_{t-}$  for a cadlag process N. Rytgaard et al. (2022) give their likelihood as

$$\begin{split} dP(O) &= \underset{t \in [0,\tau]}{\pi} \Big( d\Lambda^a(t) (\pi_t(1))^{\mathbb{I}\{A(t)=1\}} (1-\pi_t(1))^{\mathbb{I}\{A(t)=0\}} \Big)^{\Delta N^a(t)} (1-d\Lambda^a(t))^{1-\Delta N^a(t)} \\ &\times \underset{t \in [0,\tau]}{\pi} \Big( d\Lambda^d(t) \Big)^{\Delta N^d(t)} \Big( 1-d\Lambda^d(t) \Big)^{1-\Delta N^d(t)} \\ &= \underset{t \in [0,\tau]}{\pi} \Big( (\pi_t(1))^{\mathbb{I}\{A(t)=1\}} (1-\pi_t(1))^{\mathbb{I}\{A(t)=0\}} \Big)^{\Delta N^a(t)} \\ &\times \underset{t \in [0,\tau]}{\pi} (d\Lambda^a(t))^{\Delta N^a(t)} (1-d\Lambda^a(t))^{1-\Delta N^a(t)} \Big( d\Lambda^d(t) \Big)^{\Delta N^d(t)} \Big( 1-d\Lambda^d(t) \Big)^{1-\Delta N^d(t)} \\ &= \underset{t \in [0,\tau]}{\pi} dG_t dQ_t \end{split}$$

where

$$dG_t = \left( (\pi_t(1))^{\mathbb{1}\{A(t) = 1\}} (1 - \pi_t(1))^{\mathbb{1}\{A(t) = 0\}} \right)^{\Delta N^a(t)}$$

$$dQ_t = \left(d\Lambda^a(t)\right)^{\Delta N^a(t)} \left(1 - d\Lambda^a(t)\right)^{1 - \Delta N^a(t)} \left(d\Lambda^d(t)\right)^{\Delta N^d(t)} \left(1 - d\Lambda^d(t)\right)^{1 - \Delta N^d(dt)}$$

Let  $dG_t^* = \left((1)^{\mathbb{I}\{A(t)=1\}}(0)^{\mathbb{I}\{A(t)=0\}}\right)^{\Delta N^a(t)} = \left((0)^{\mathbb{I}\{A(t)=0\}}\right)^{\Delta N^a(t)}$ , corresponding to staying on treatment. Then define the interventional density as

$$dP_{Q,G^*}(O) = \pi_{t \in [0,\tau]} dG_t^* dQ_t$$

and their target estimand  $\Psi_t^{\text{Rytgaard}}: \mathcal{M} \to \mathbb{R}_+$  as

$$\Psi_{\tau}^{\text{Rytgaard}}(P) = \mathbb{E}_{P_{Q,G^*}}[N_{\tau}^d] = \int_{\mathcal{O}} y \underset{t \in (0,\tau]}{\pi} dG_t^* dQ_t \tag{2}$$

We first need to define the integral in Equation 2. To get a fully rigorous result, consider Proposition 1 in Ryalen (2024) and Theorem 8.1.2 in Last & Brandt (1995).

First note that we have

$$\underset{t \in (0,\tau]}{\pi} dG_t^* dQ_t = \underset{t \in \left(0,t_{(1)}\right]}{\pi} dG_t^* dQ_t \underset{t \in \left(t_{(1)},\tau\right]}{\pi} dG_t^* dQ_t \mathbb{1}\{t_1 < t_2\}$$

Let  $Y_{\tau} = \mathbbm{1} \left\{ T_{(1)} \leq \tau, D_{(1)} = 03 \right\} + \mathbbm{1} \left\{ T_{(2)} \leq \tau \right\} \coloneqq Y_{\tau}^{(1)} + Y_{\tau}^{(2)}$  be death at time  $\tau$ . Then, note that

$$y_{\tau}^{(1)}(t_1,d_1) \underset{t \in \left(0,t_{(1)}\right]}{\pi} dG_t^* dQ_t \underset{t \in \left(t_{(1)},\tau\right]}{\pi} dG_t^* dQ_t \mathbb{1}\{t_1 < t_2\} = y_{\tau}^{(1)} \underset{t \in \left(0,t_{(1)}\right]}{\pi} dG_t^* dQ_t$$

The second product integral evaluates to 1 because death at event 1 implies that all intensities are 0 after the first event.

We find

$$\begin{split} \pi_{t \in \left(0, t_{(1)}\right]} dG_t^* dQ_t &= \left((0)^{\mathbb{I}\{d_1 = 02\}}\right)^{\mathbb{I}\{d_1 \in \{01, 02\}\}} (d\Lambda^a(t_1))^{\mathbb{I}\{d_1 \in \{01, 02\}\}} \left(d\Lambda^d(t_1)\right)^{\mathbb{I}\{d_1 = 03\}} \\ &\times \pi_{t \in \left(0, t_{(1)}\right)} \left(1 - d\Lambda^d(t)\right) (1 - d\Lambda^a(t)) \\ &= (d\Lambda^a(t_1))^{\mathbb{I}\{d_1 \in \{01\}\}} (0dt_1)^{\mathbb{I}\{d_1 \in \{02\}\}} \left(d\Lambda^d(t_1)\right)^{\mathbb{I}\{d_1 = 03\}} S_0(t_1 -) \\ &= \left((h^{01}(t_1) + h^{02}(t_1))dt_1\right)^{\mathbb{I}\{d_1 \in \{01\}\}} (0dt_1)^{\mathbb{I}\{d_1 \in \{02\}\}} \left(h^{03}(t_1)dt_1\right)^{\mathbb{I}\{d_1 = 03\}} S_0(t_1 -) \\ &= S_0(t_1 -) \mathbb{I}\{d_1 = 01\} (h^{01}(t_1) + h^{02}(t_1))dt_1 \\ &+ S_0(t_1 -) \mathbb{I}\{d_1 = 03\} h^{03}(t_1)dt_1 \end{split}$$

(compare with Equation (11) in Ryalen (2024)). In the second equality, we used that the counting processes do not jump at the same time with probability one to get  $S(t_1) = \pi t \in (0, t_{(1)}]$ 

 $d\Lambda^d(t)\big)(1-d\Lambda^a(t)).$  But multiplying with  $y_{\tau}^{(1)},$  we find

$$y_{\tau}^{(1)} \pi_{t \in (0,t_{(1)}]} dG_t^* dQ_t = y_{\tau}^{(1)} S(t_1 -) \mathbb{1}\{d_1 = 03\} h^{03}(t_1) dt_1$$

Therefore, we have

$$\int y_{\tau}^{(1)} \underset{t \in (0,t_{(1)}]}{\pi} dG_t^* dQ_t = \int_0^{\tau} S(s-)h^{03}(s) ds$$

Similarly, we may find

$$\begin{split} y_{\tau}^{(2)} & \underbrace{\pi}_{t \in \left(0, t_{(1)}\right]} dG_{t}^{*} dQ_{t} \underbrace{\pi}_{t \in \left(t_{(1)}, t_{(2)}\right]} dG_{t}^{*} dQ_{t} \mathbb{1}\{t_{1} < t_{2}\} \\ &= y_{\tau}^{(2)} \mathbb{1}\{t_{1} < t_{2}\} S(t_{1} -) \mathbb{1}\{d_{1} = 01\} \left(h^{01}(t_{1}) + h^{02}(t_{1})\right) \\ & \times S(t_{2} - \mid 01, t_{1}) h^{13}(t_{1}, t_{2}) dt_{2} dt_{1} \end{split}$$

Thus the target estimand is

$$\begin{split} \Psi_{\tau}^{\text{Rytgaard}}(P) &= \int_{0}^{\tau} S_{0}(s-)h^{03}(s)ds \\ &+ \int_{0}^{\tau} S_{0}(s-)P_{13}(\tau \mid 01,s) \big(h^{01}(s) + h^{02}(s)\big)ds \end{split} \tag{3}$$

## 4.2 Comparison of the approaches

We are now in a position, where we can readily compare the approaches in Rytgaard et al. (2022) and Ryalen (2024) by considering the difference between Equation 3 and Equation 1.

Suppose that  $h^{02}(s) > 0$  and  $h^{13}(s,w) > 0$  for Lebesgue almost all s,w. From this, we conclude that  $\Psi_{\tau}^{\text{Rytgaard}}(P) = \Psi_{\tau}^{\text{Ryalen}}(P)$  if and only if  $h^{02} \equiv 0$  a.e. if and only if  $\pi_t(1) \equiv 1$  a.e. (with respect to the Lebesgue measure restricted to  $[0,\tau]$ ). To see this, note that

$$\begin{split} \Psi_{\tau}^{\text{Ryalen}}(P) - \Psi_{\tau}^{\text{Rytgaard}}(P) &= \int_{0}^{\tau} \exp\left(-\sum_{j \neq 2} \int_{0}^{s} h^{0j}(u) du\right) \left(1 - \exp\left(-\int_{0}^{s} h^{02}(u) du\right)\right) h^{03}(s) ds \\ &+ \int_{0}^{\tau} \exp\left(-\sum_{j \neq 2} \int_{0}^{s} h^{0j}(u) du\right) P_{13}(\tau \mid 01, s) \\ & \times \left(1 - \exp\left(-\int_{0}^{s} h^{02}(u) du\right)\right) h^{01}(s) ds \\ &+ \int_{0}^{\tau} S_{0}(s -) P_{13}(\tau \mid 01, s) h^{02}(s) ds \end{split} \tag{4}$$

Since each term is non-negative,  $\Psi_{\tau}^{\text{Rytgaard}}(P) = \Psi_{\tau}^{\text{Ryden}}(P)$  implies that each term is equal to zero. Since each of the integrands are non-negative, we must have that the integrands are equal to zero (almost surely). By letting  $m_{[0,\tau]}$  denote the Lebesgue measure on  $[0,\tau]$ , we have for the first term in Equation 4,

$$\begin{split} \exp\bigg(-\sum_{j\neq 2}\int_0^s h^{0j}(u)du\bigg) \bigg(1-\exp\bigg(-\int_0^s h^{02}(u)du\bigg)\bigg)h^{03}(s) &= 0 \quad m_{[0,\tau]} - \text{almost all } s \Leftrightarrow \\ \bigg(1-\exp\bigg(-\int_0^s h^{02}(u)du\bigg)\bigg)h^{03}(s) &= 0 \quad m_{[0,\tau]} - \text{almost all } s \Leftrightarrow \\ \bigg(1-\exp\bigg(-\int_0^s h^{02}(u)du\bigg)\bigg) &= 0 \quad m_{[0,\tau]} - \text{almost all } s \Leftrightarrow \\ h^{02}(s) &= 0 \quad m_{[0,\tau]} - \text{almost all } s \end{split}$$

with similar arguments for the second and third terms in Equation 4.

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