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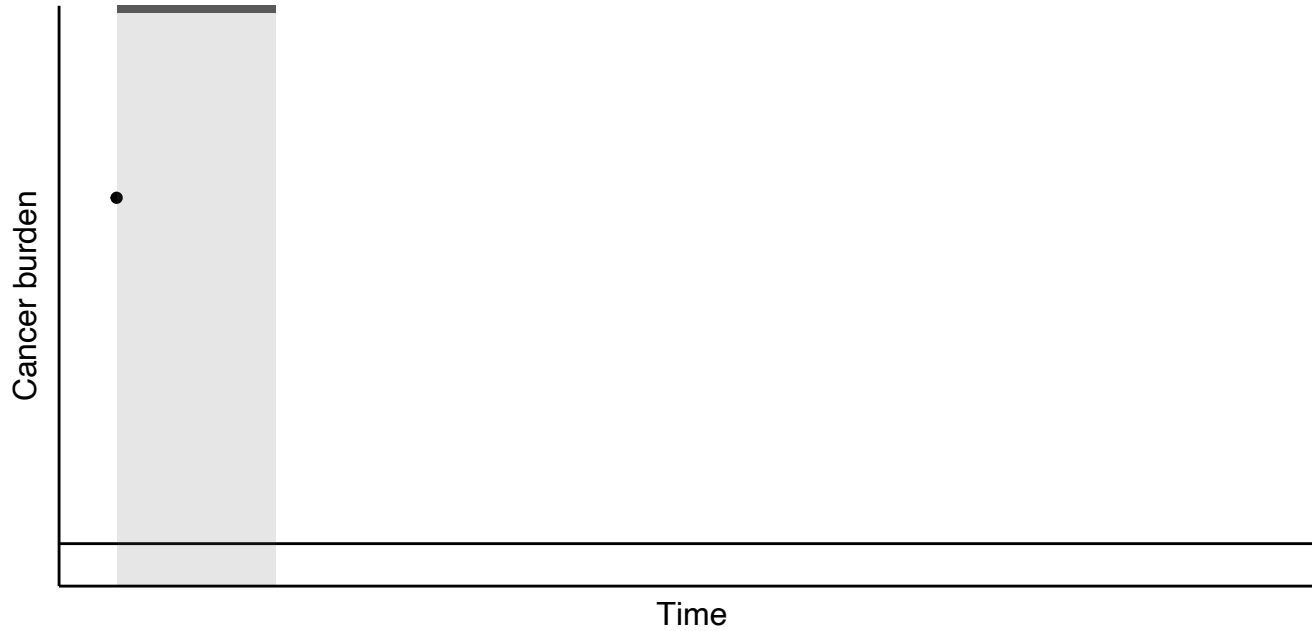
Waves of cancer and how to tackle them

Eszter Lakatos

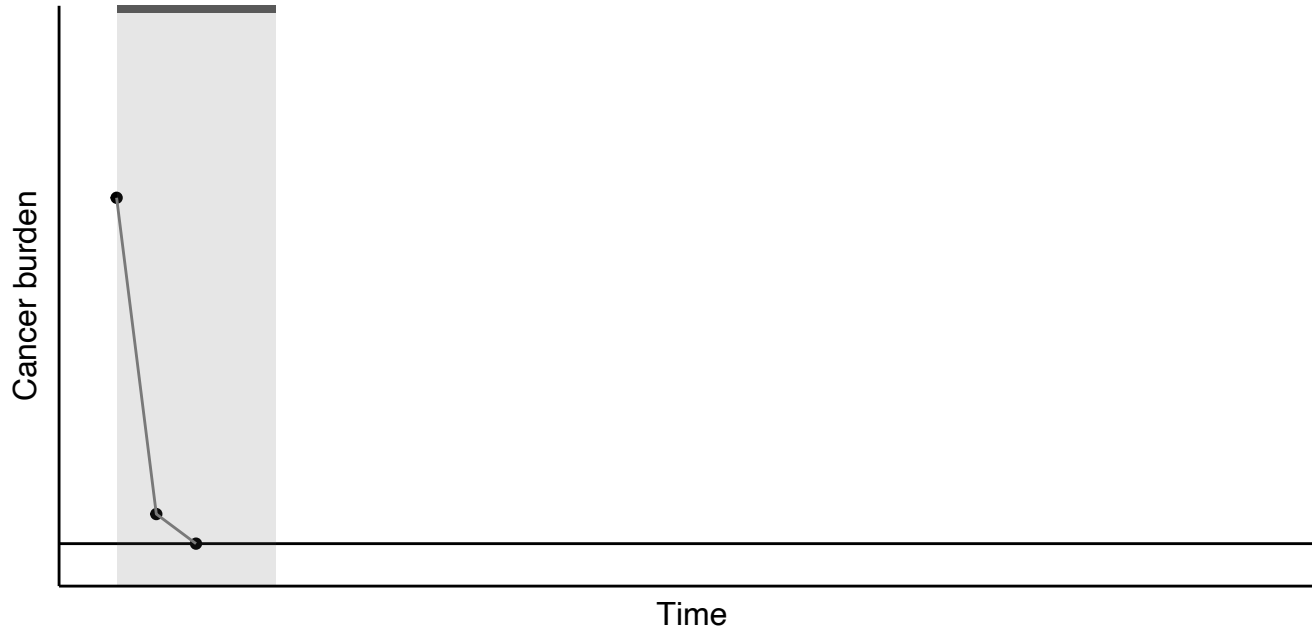
Assistant Professor

Computing Disease Evolution (CODE) group

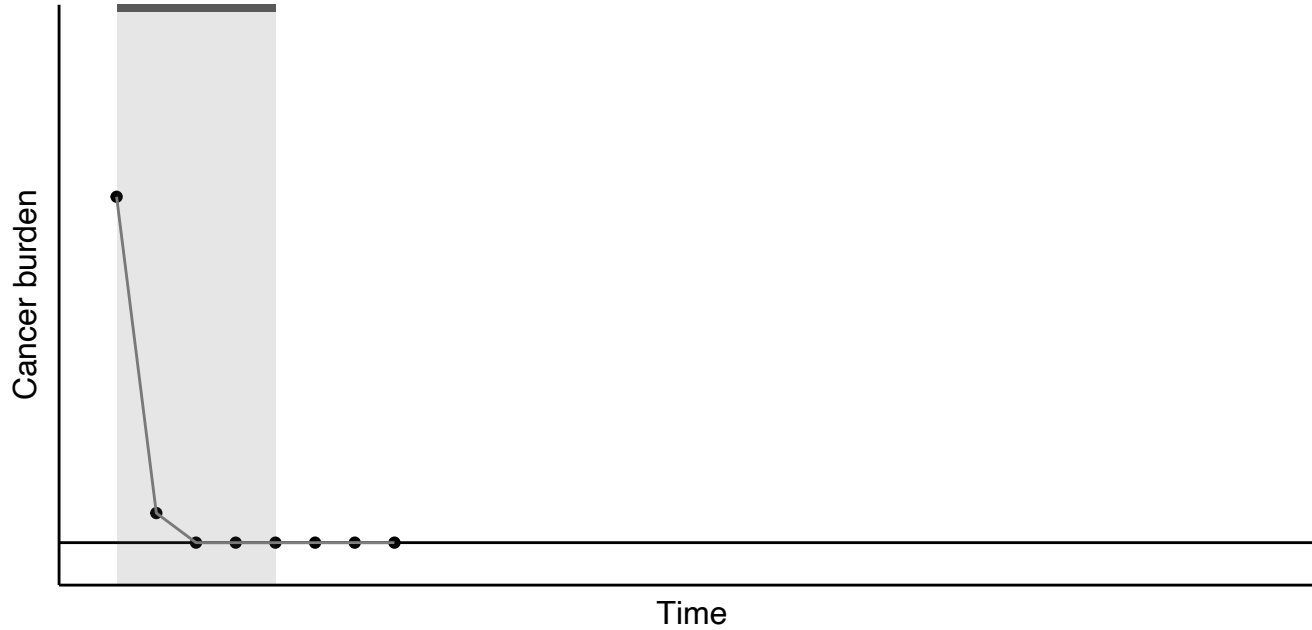
Why is cancer still a problem?



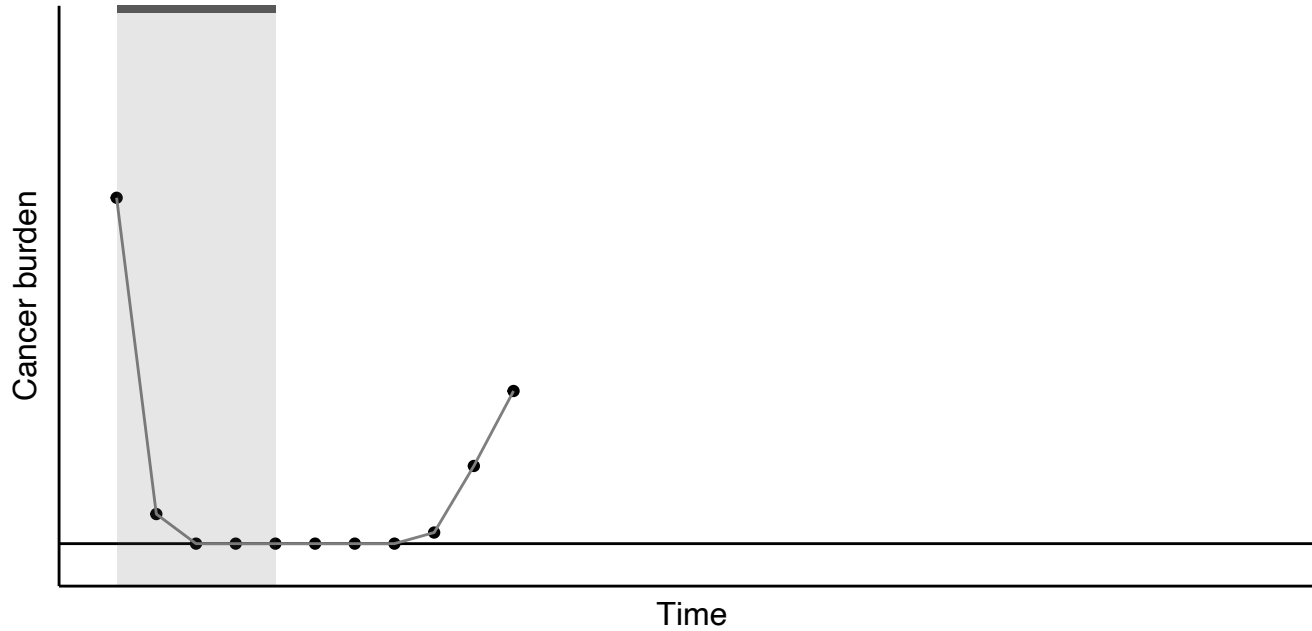
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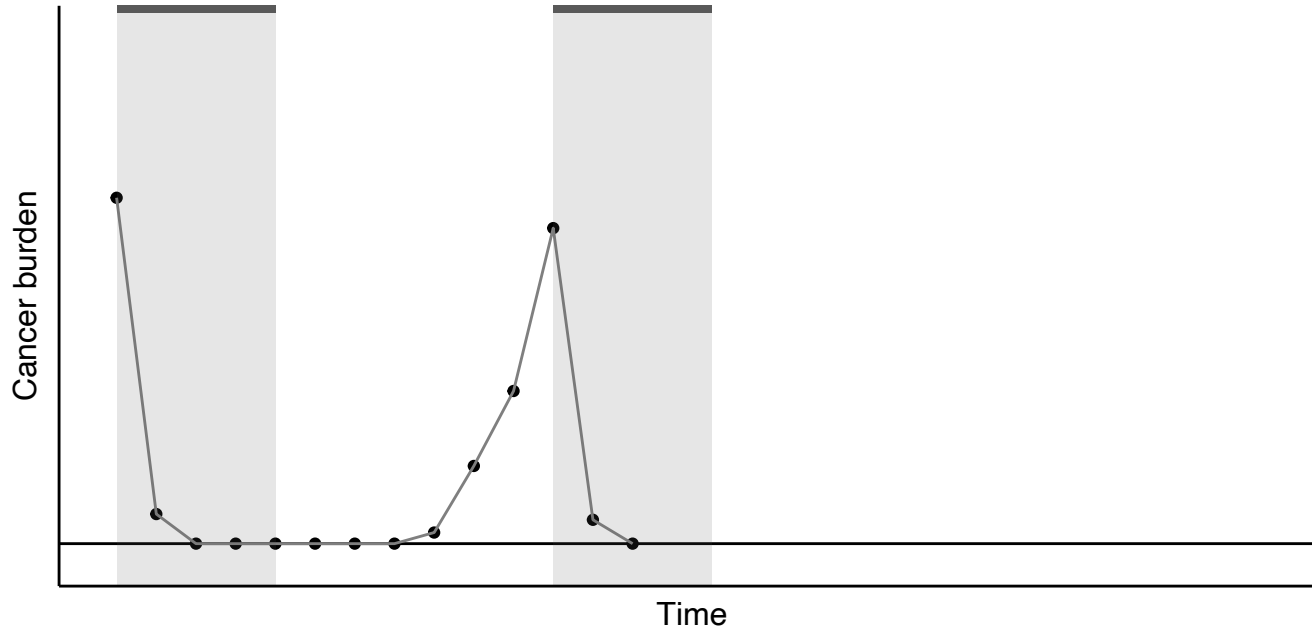
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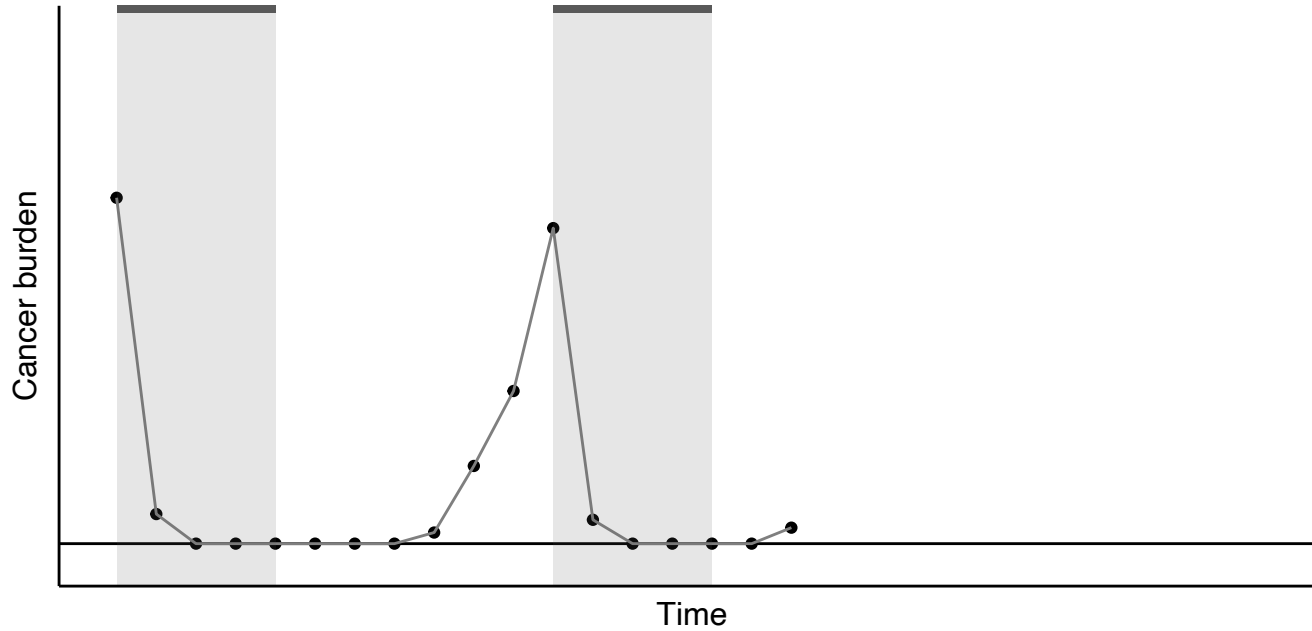
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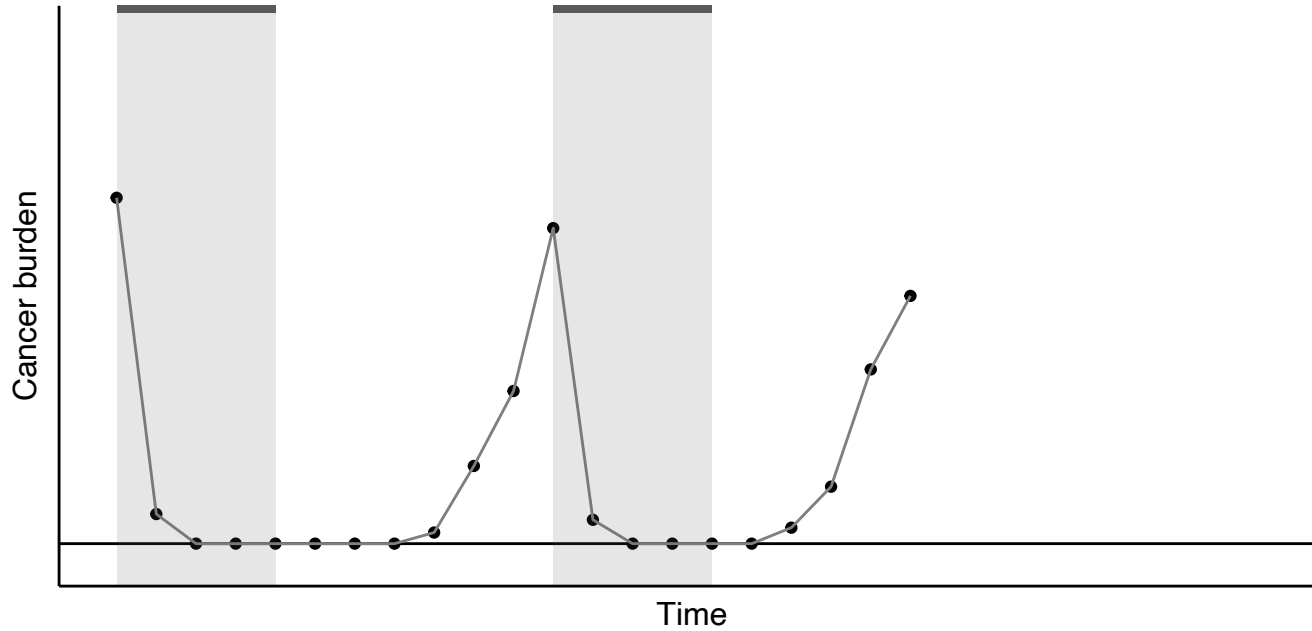
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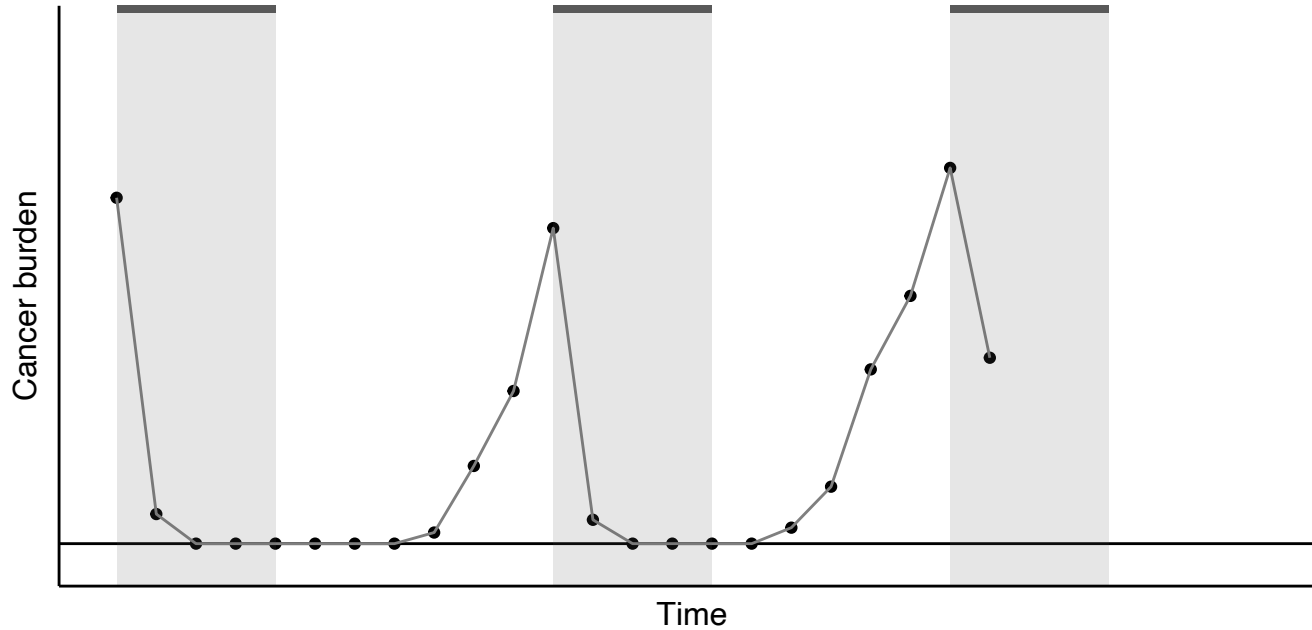
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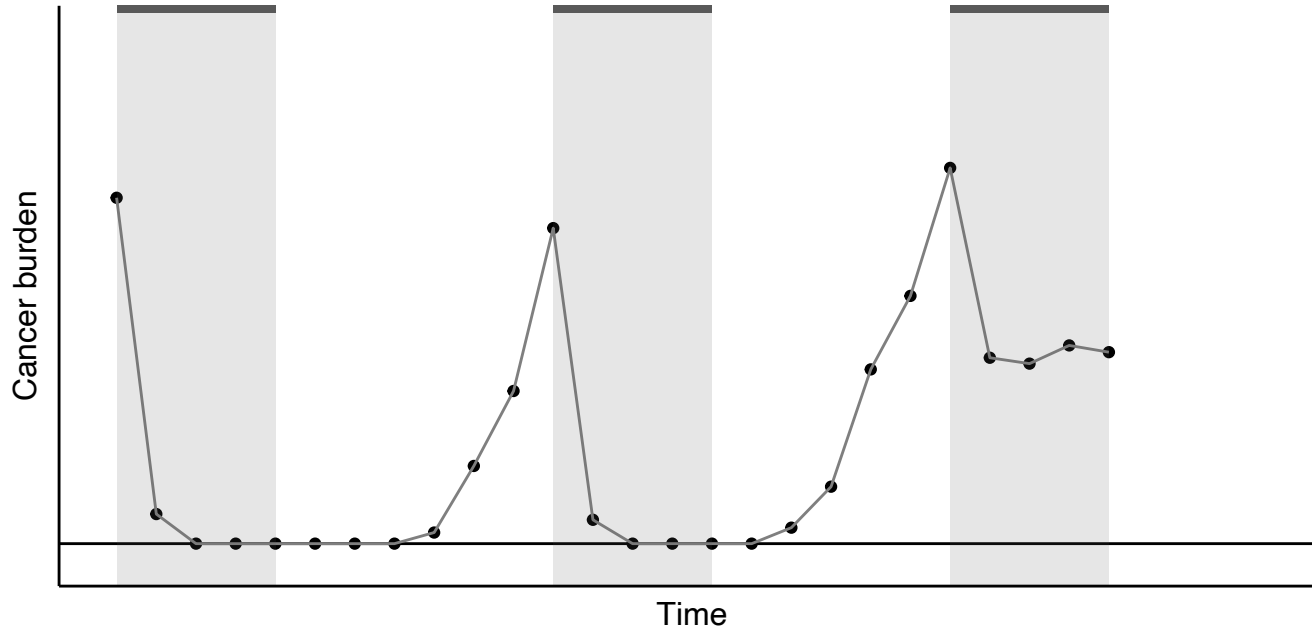
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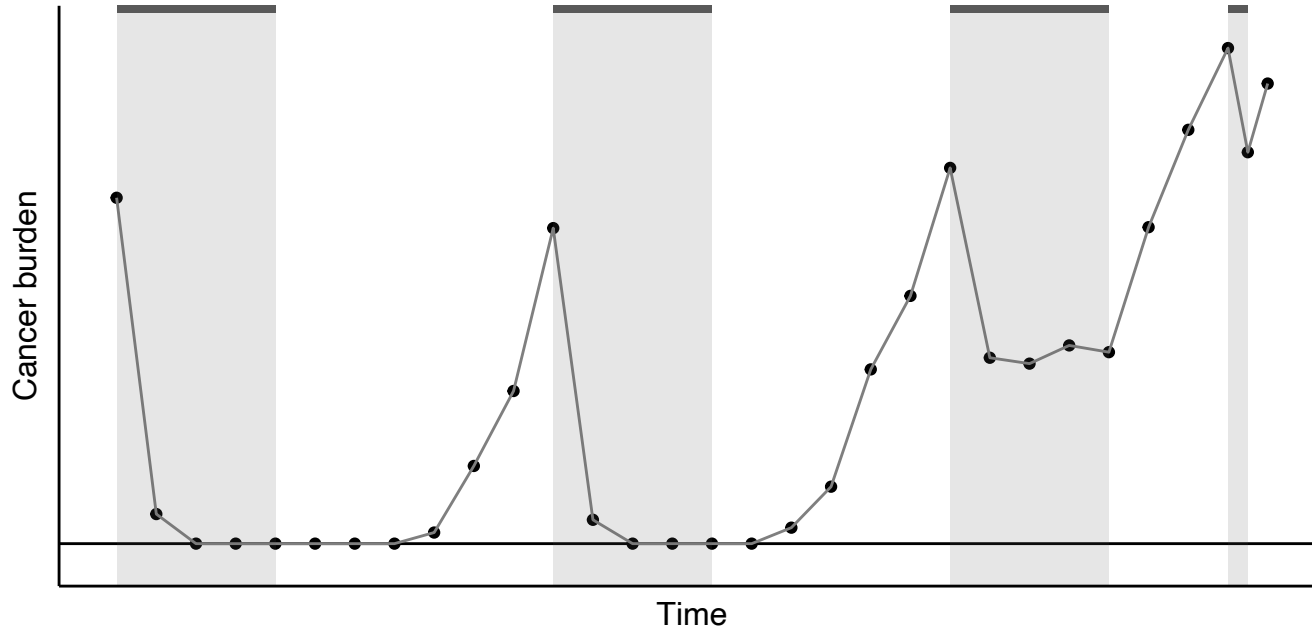
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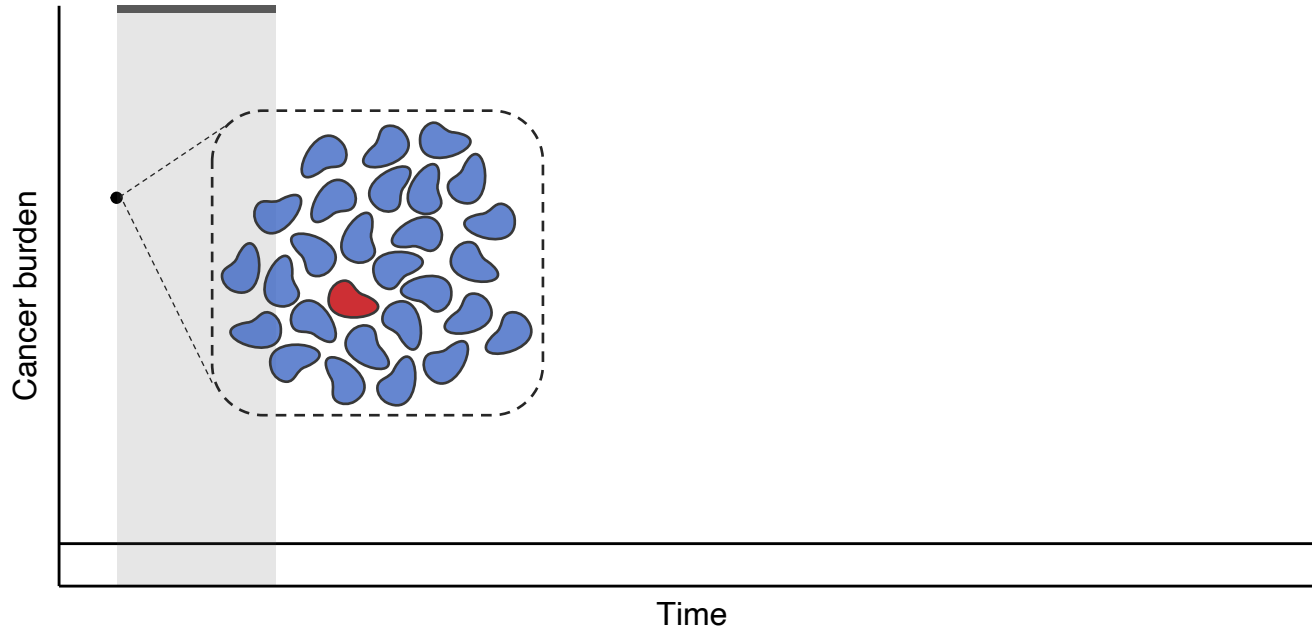
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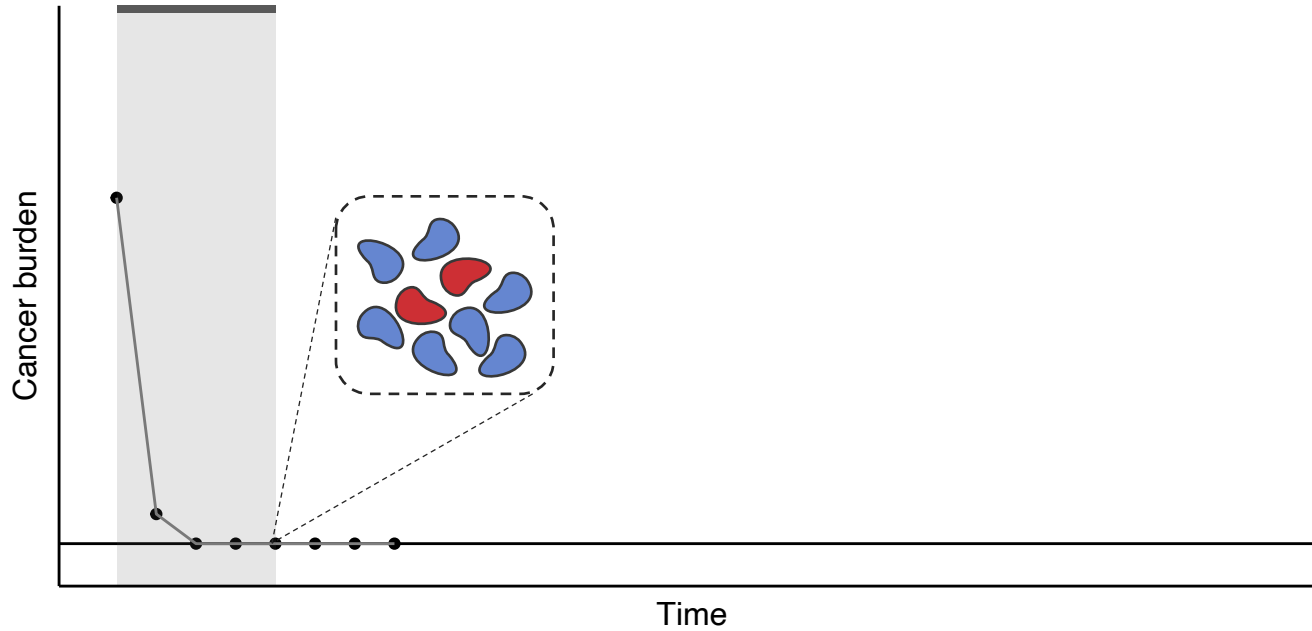
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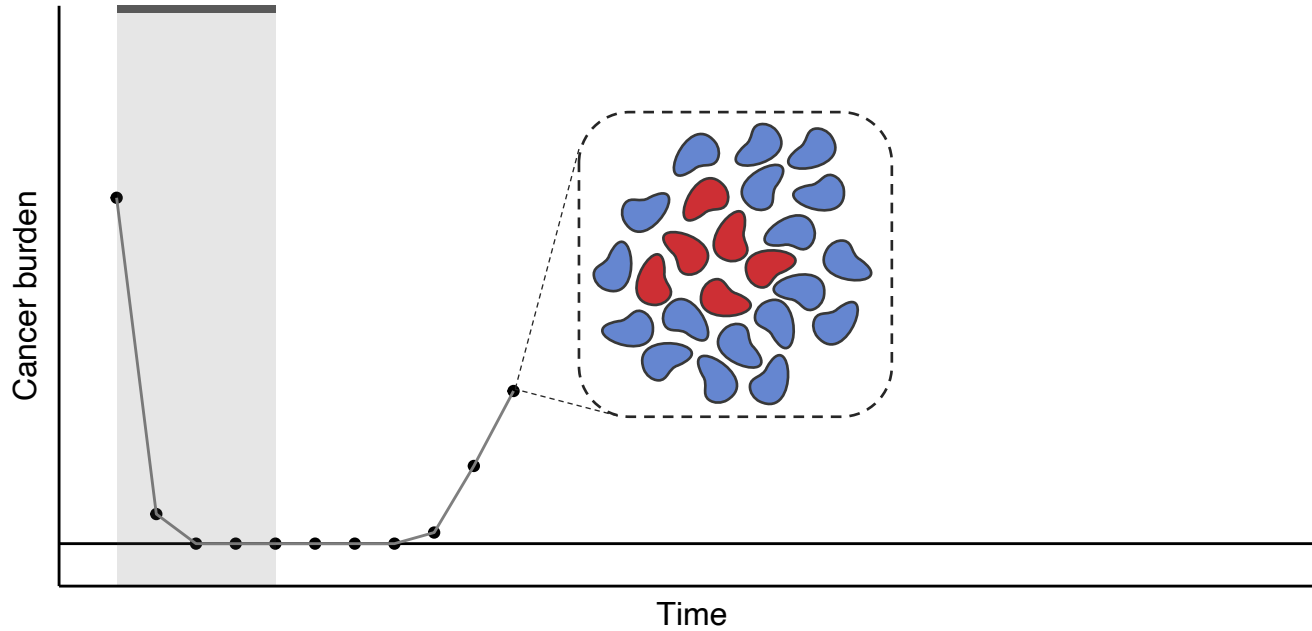
What's going on inside the cancer?



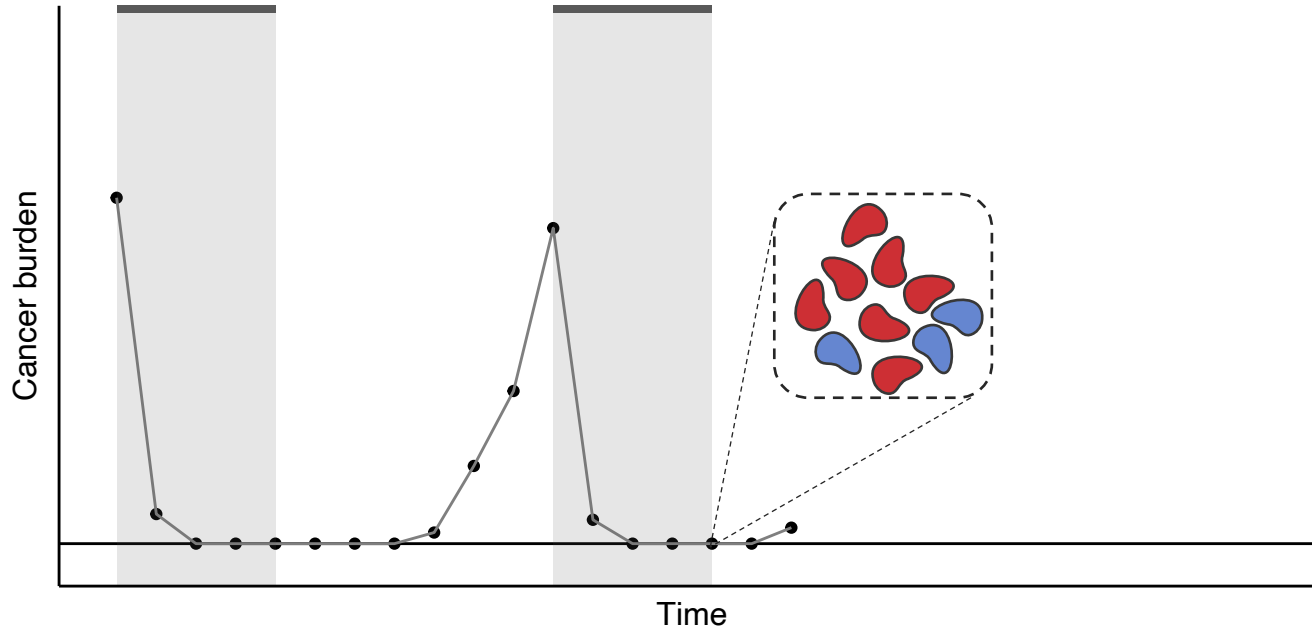
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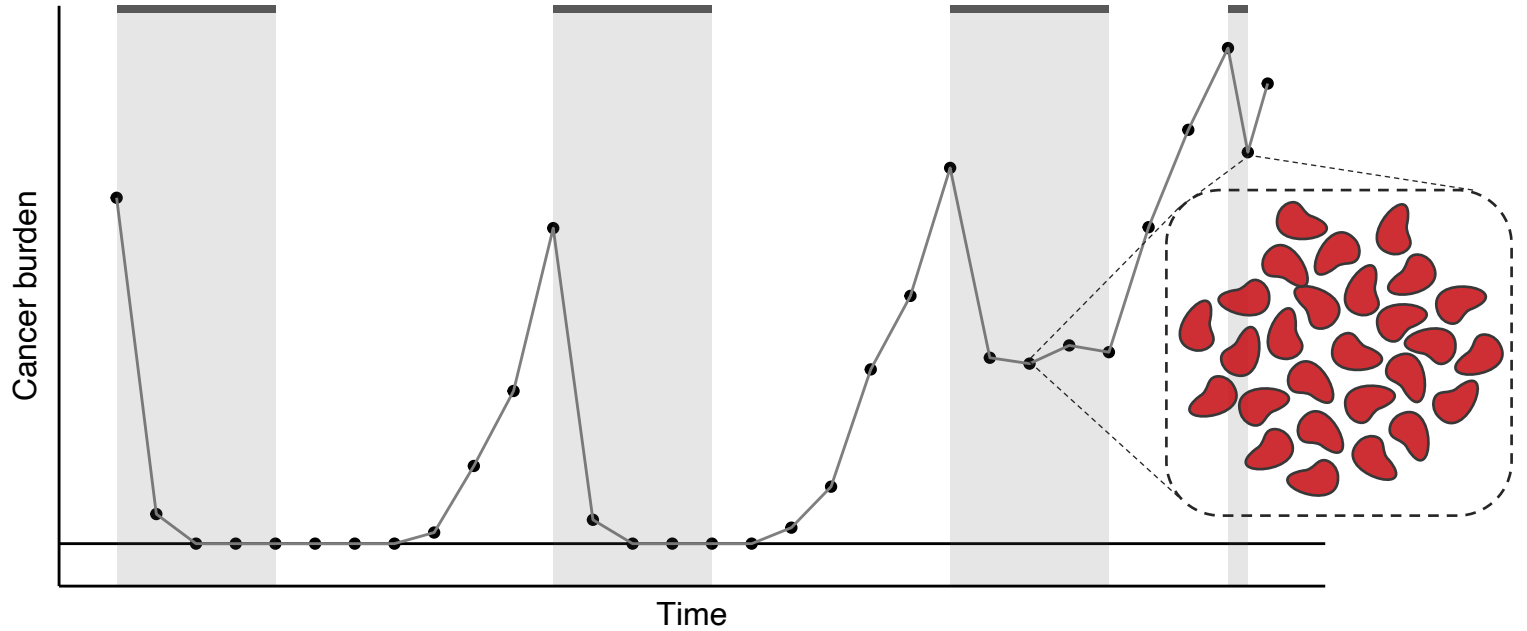
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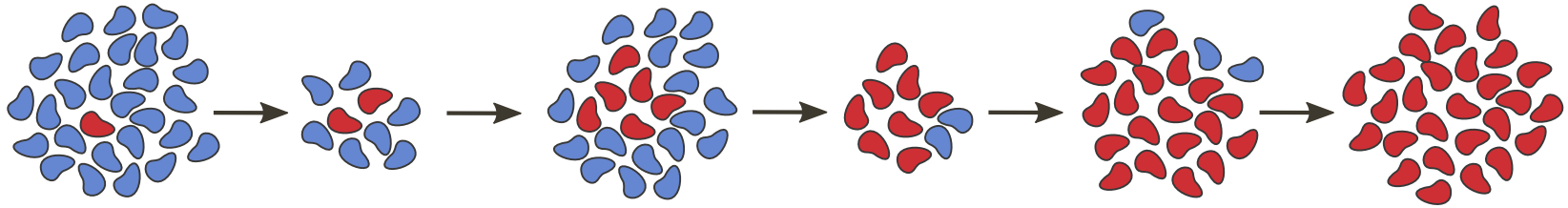
What's going on inside the cancer?



What's going on inside the cancer?



What can we (mathematicians) do?



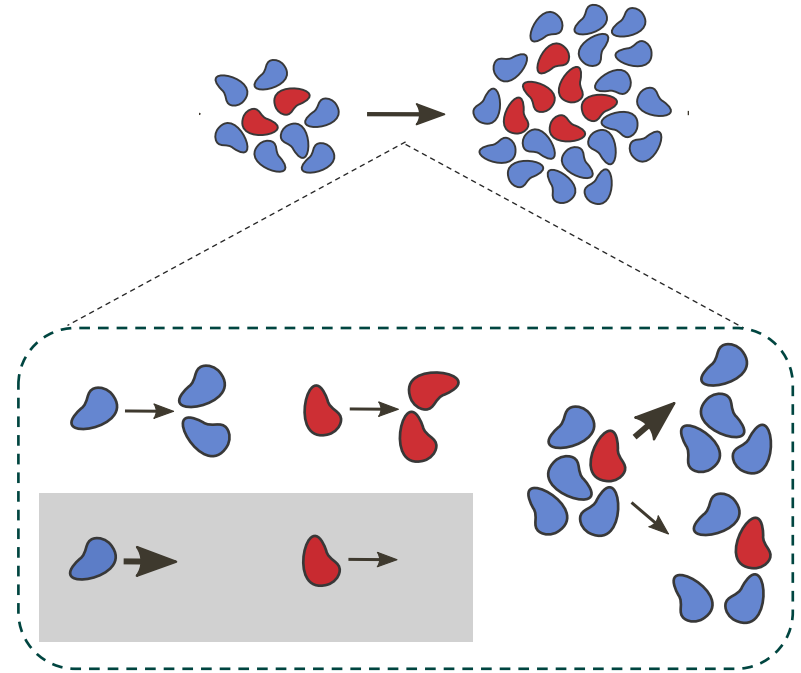
- We know the basic rules of what is happening
- But we cannot look inside the cancer
- And we should not try different treatments on actual patients

- We can use theory from ecology and evolutionary biology
- We can build a mathematical model!



Let's build a model!

- We have sensitive and resistant cells
- Cells continuously give birth to new cells
- Sensitive and resistant cells compete for resources
 - Limited number of cells can live
 - If too many cells are growing, cells start dying
 - Sensitive cells are stronger
- Under therapy, cells die
 - Sensitive cells die much faster
- We measure the total number of cells (imperfectly)



Let's build a model!

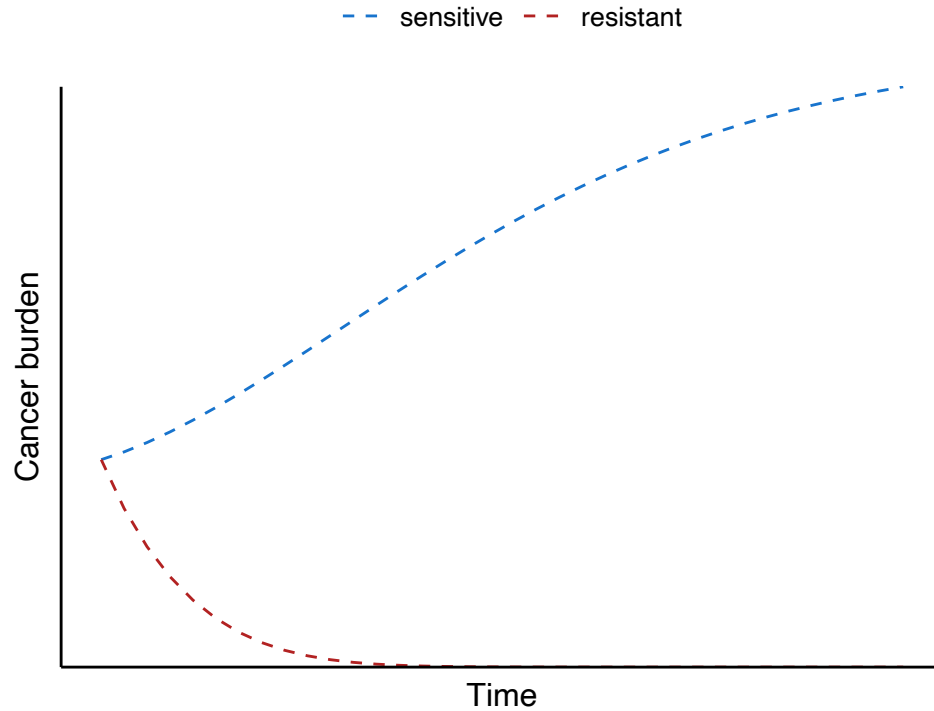
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	Proliferation (birth)	Competition	Death (therapy)
$\frac{dS}{dt}$	$b \cdot S$	$- b \cdot S \cdot \frac{S + R}{K}$	$- d_S \cdot S$
$\frac{dR}{dt}$	$b \cdot R$	$- b \cdot R \cdot \frac{c \cdot S + R}{K}$	$- d_R \cdot R$

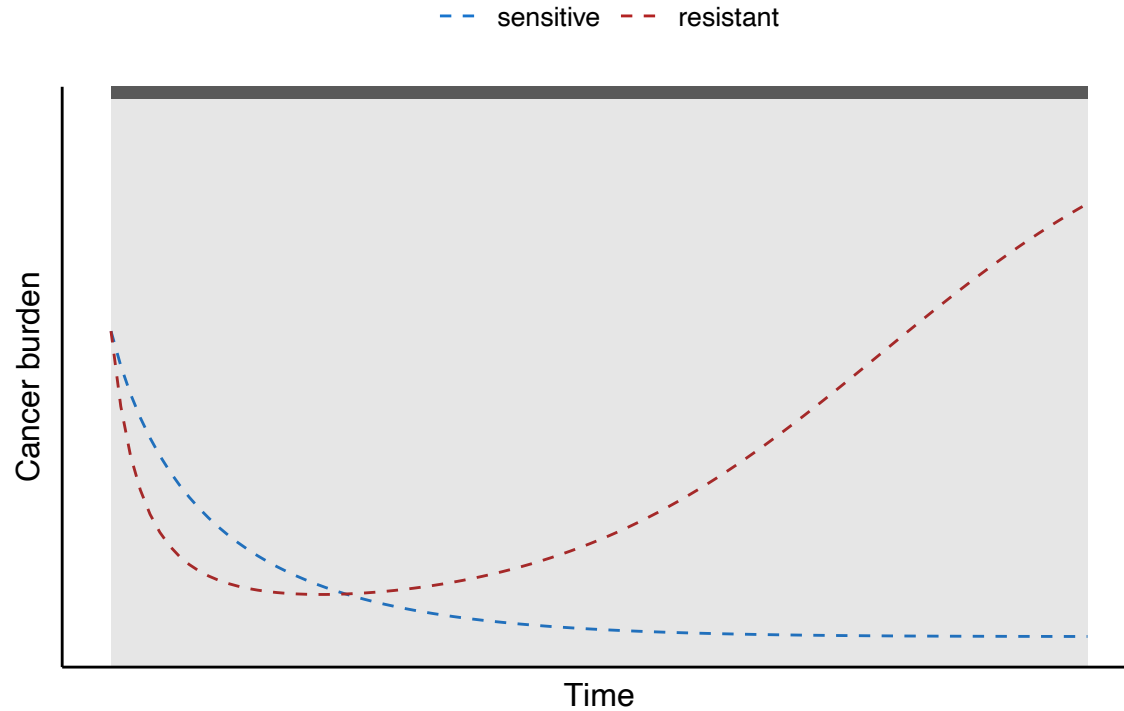
$$C = S + R + \varepsilon, \quad \varepsilon \sim \mathcal{N}(0, \sigma)$$

Cancer burden observation

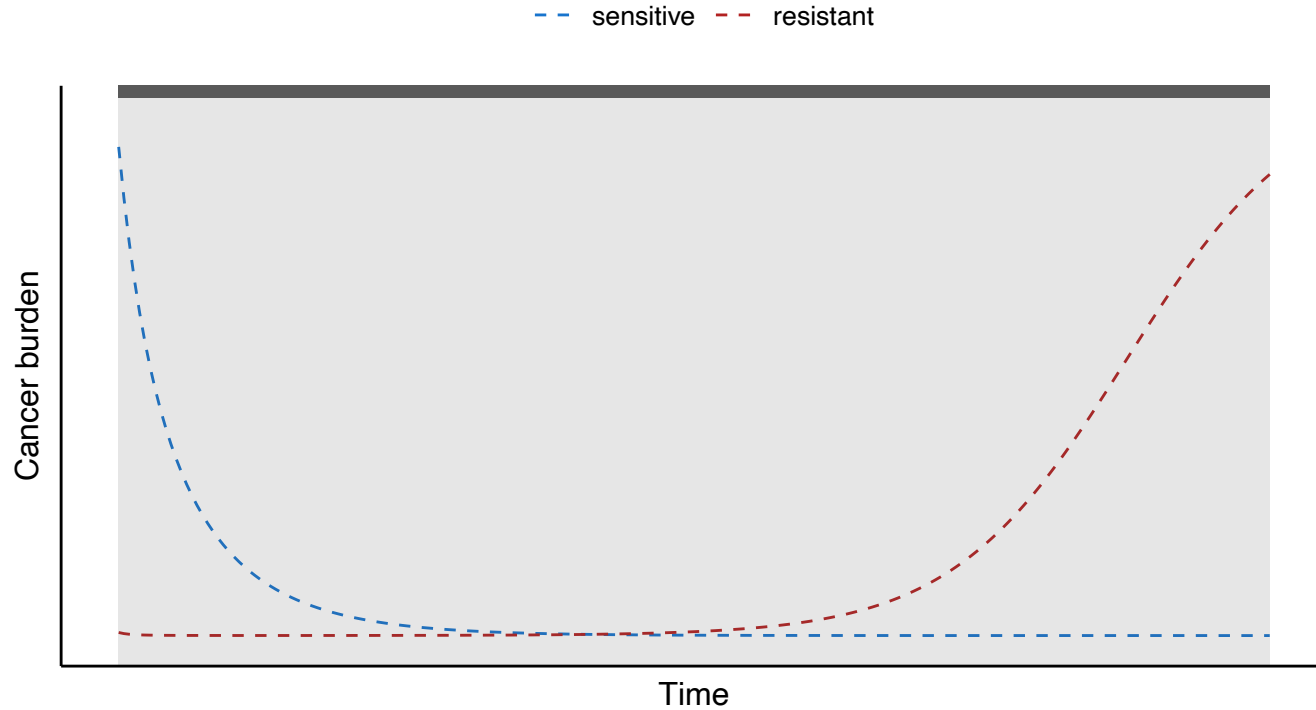
What does the model tell us?



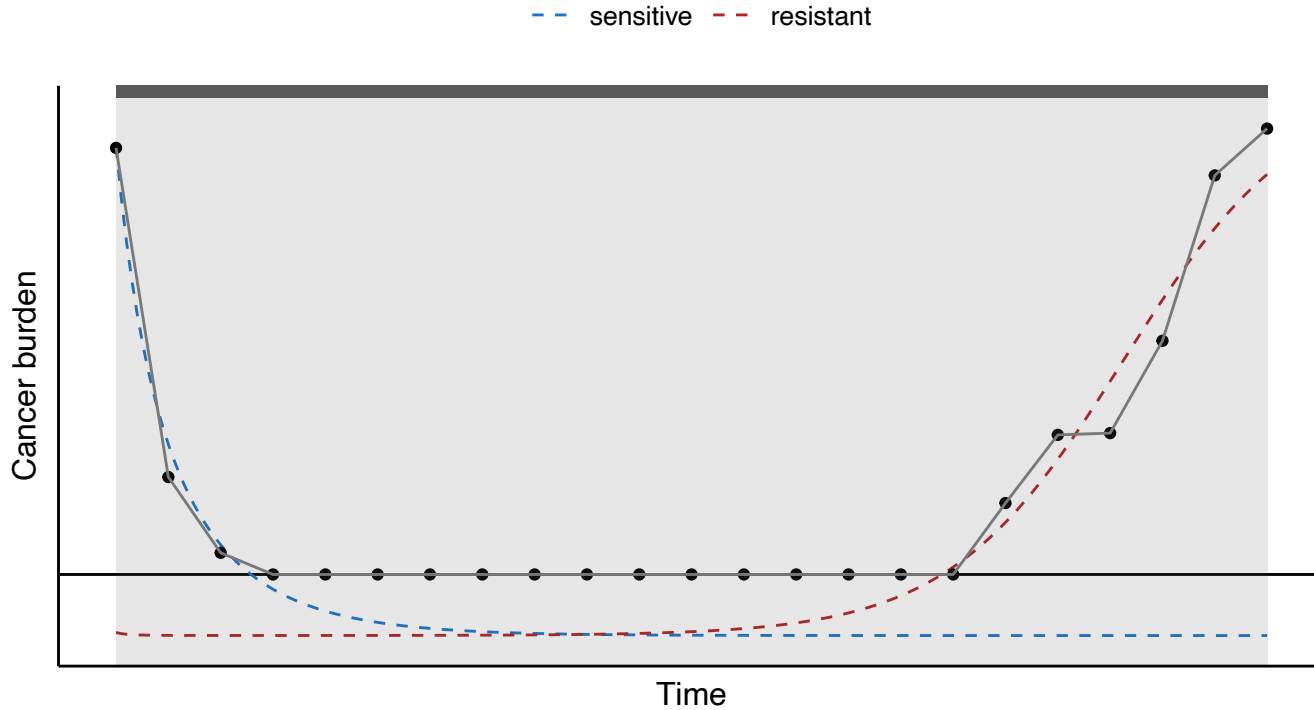
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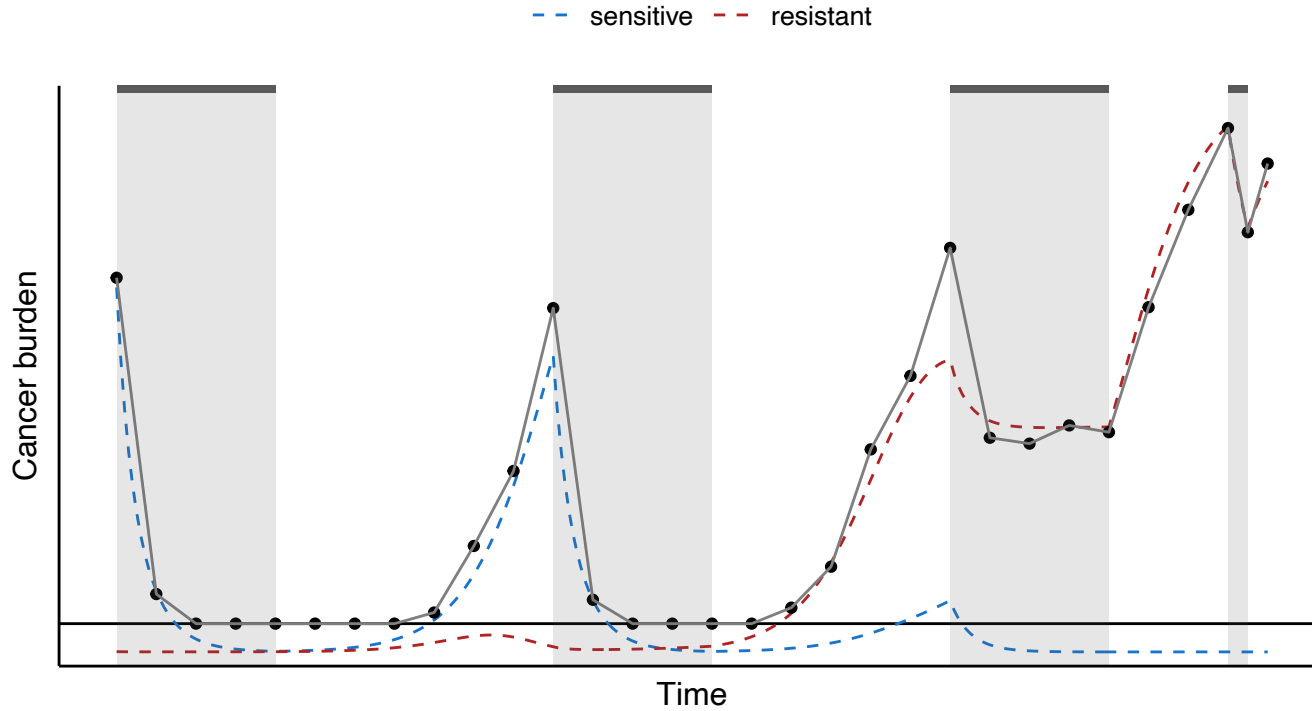
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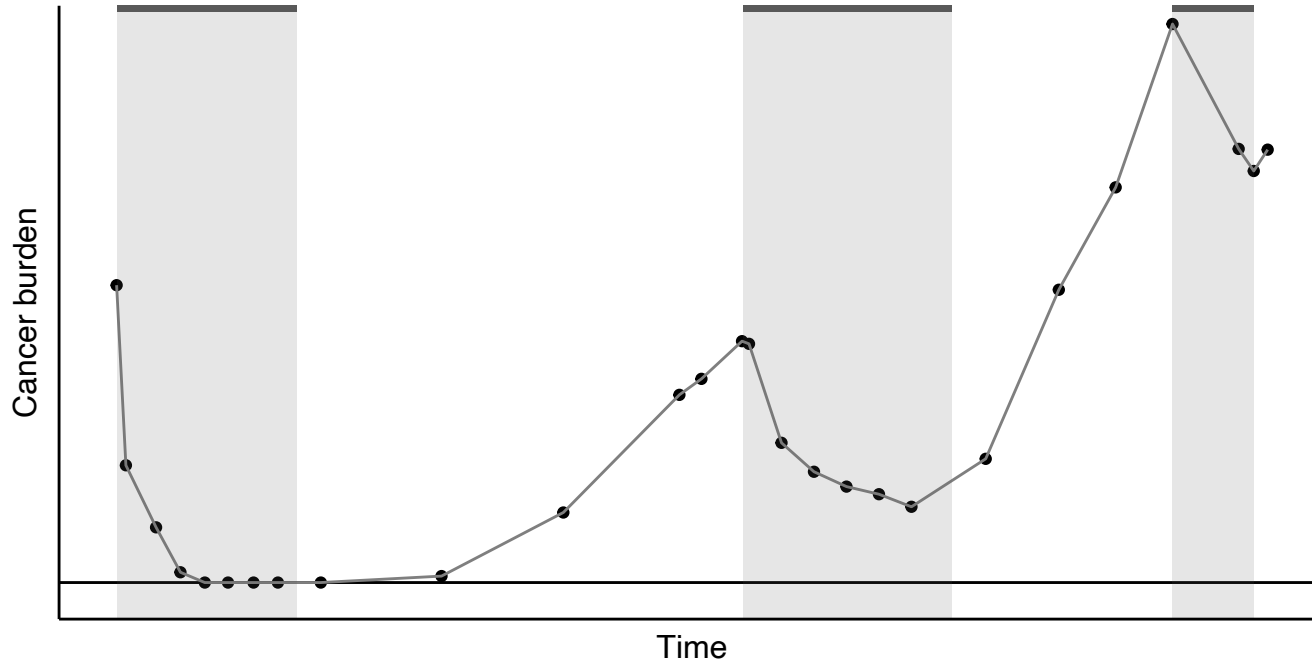


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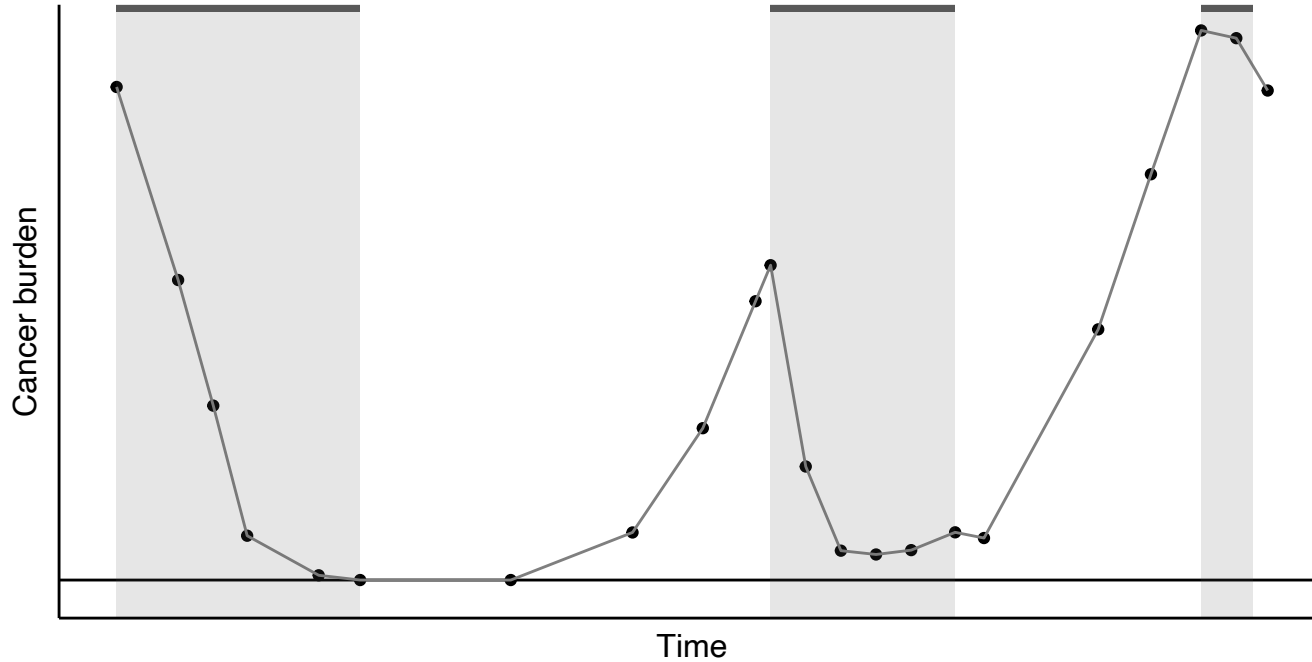
How similar is this to real life?

Patients with ovarian cancer:



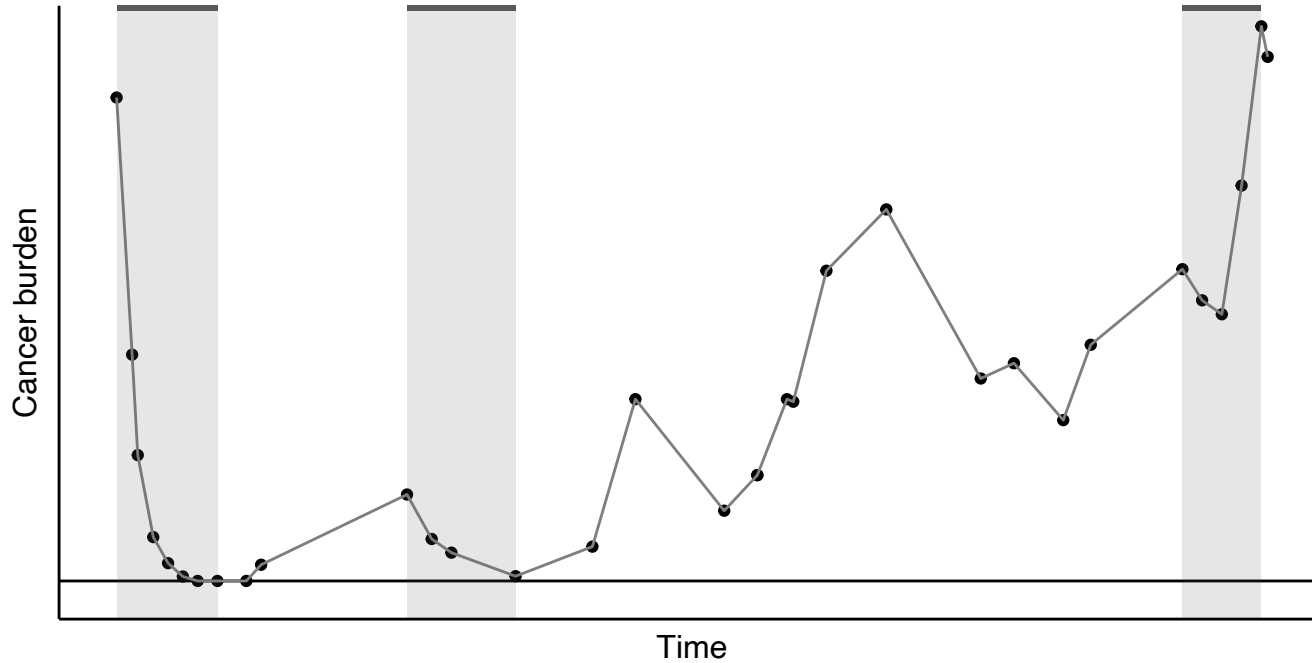
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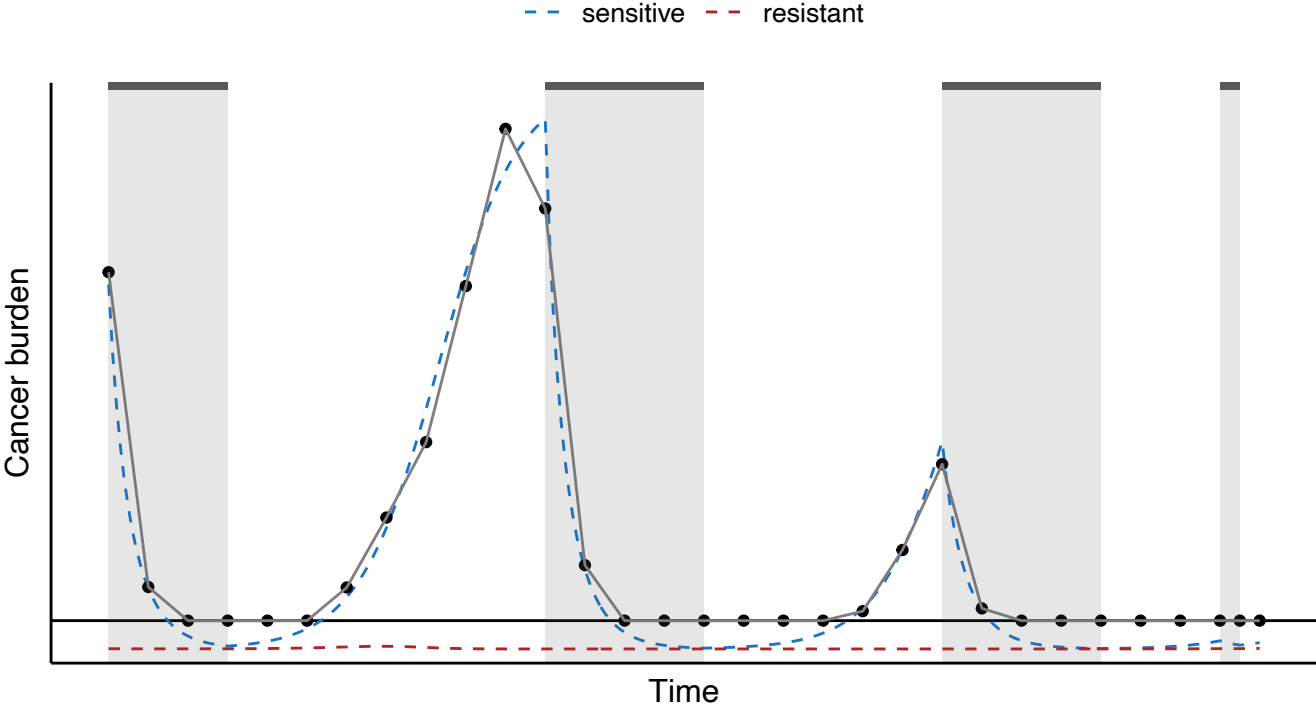


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Patients with ovarian cancer:

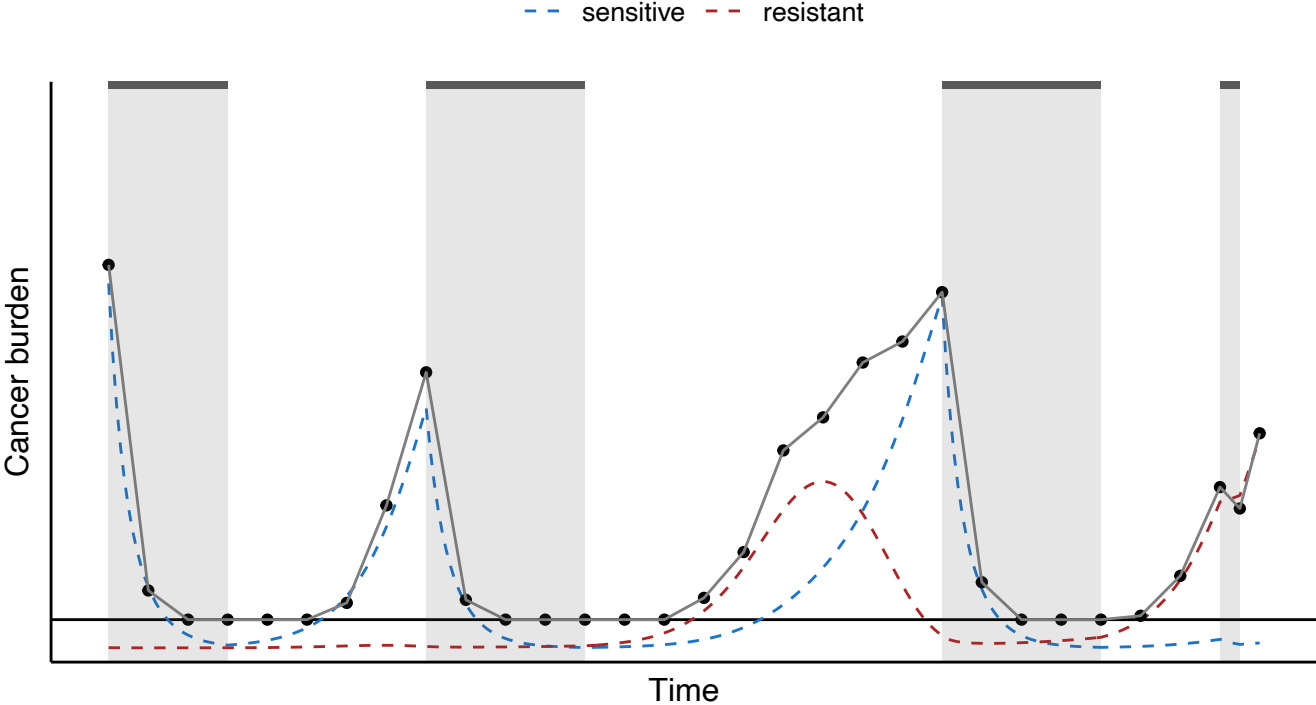


Let's make a better treatment!



total treatment: 115

Let's make a better treatment!

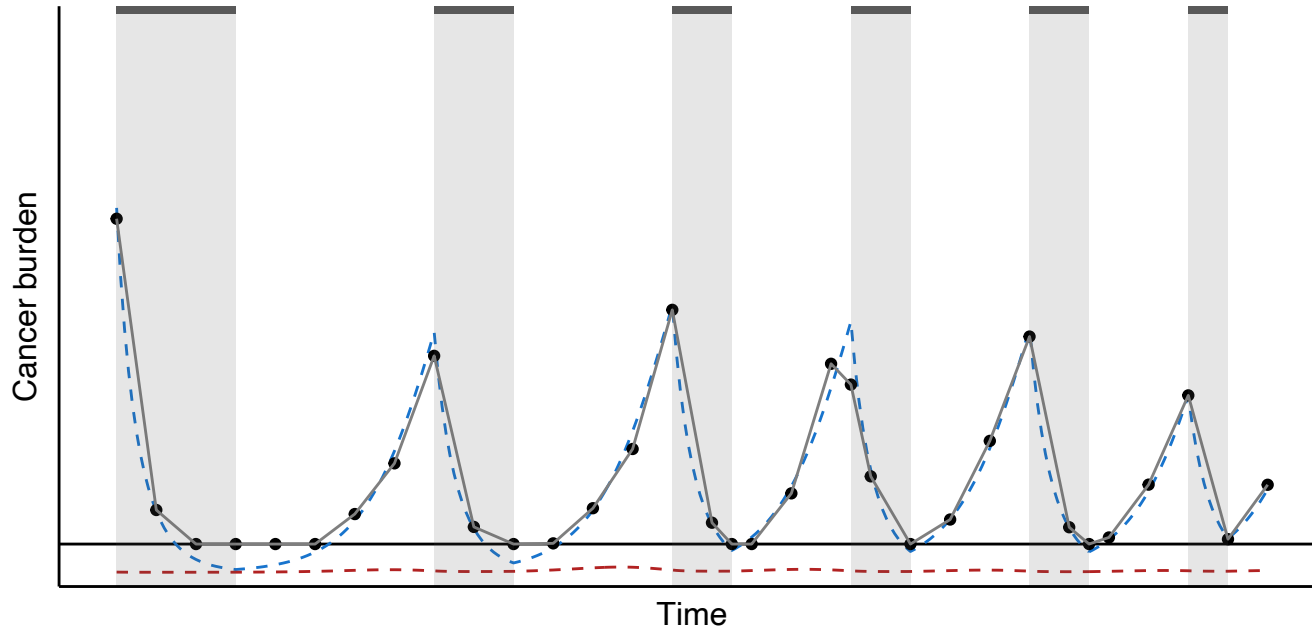


total treatment: 115

Let's make a better treatment!

Evolutionary/adaptive therapy

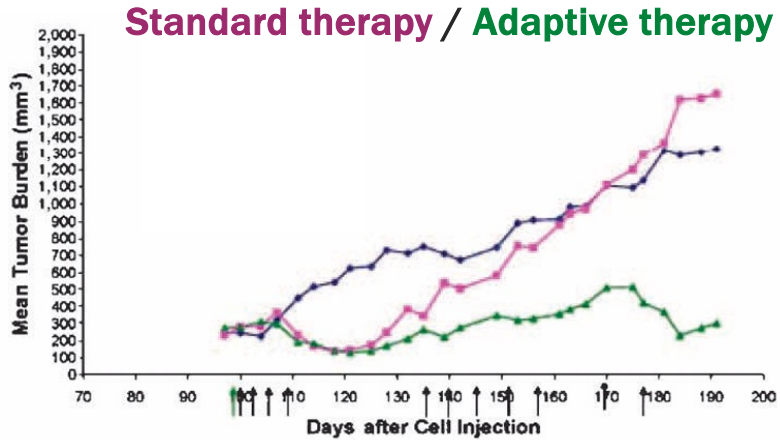
-- sensitive -- resistant



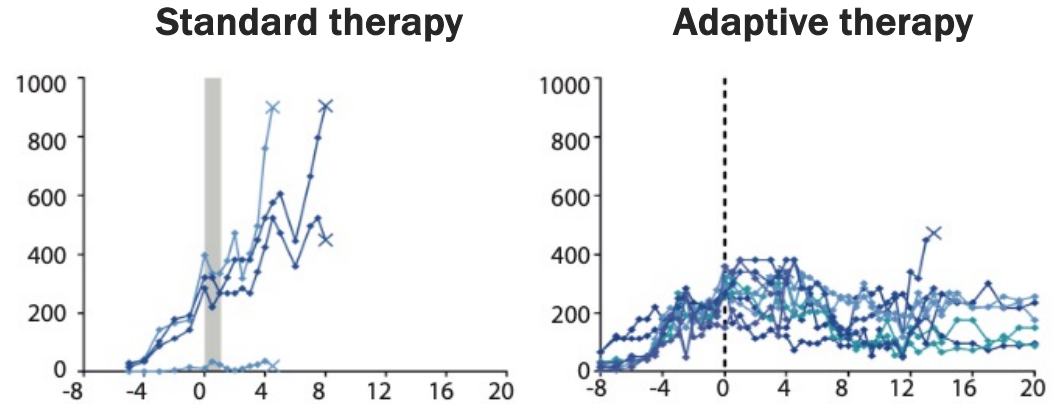
total treatment: 105

Would this really work?

Gatenby *et al.*, Cancer Research, 2009:



Hockings *et al.*, bioRxiv, 2023:



Would this really work?



ACTOV: A trial of adaptive chemotherapy in relapsed platinum-sensitive ovarian cancer

Trial at a glance

- Open trial

Cancer type: Epithelial – high-grade serous and endometrioid

Treatment stage: Recurrence

Acronym: ACTOV

Would this really work?



ACTOv: A trial of adaptive chemotherapy in relapsed platinum-sensitive ovarian cancer

ANZadapt

Prostate — Recruiting

Adaptive Abiraterone Therapy for Metastatic Castration Resistant Prostate Cancer

ClinicalTrials.gov ID ⓘ NCT02415621

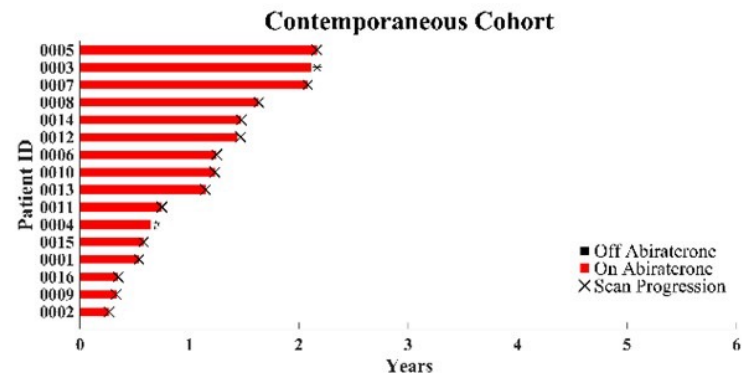
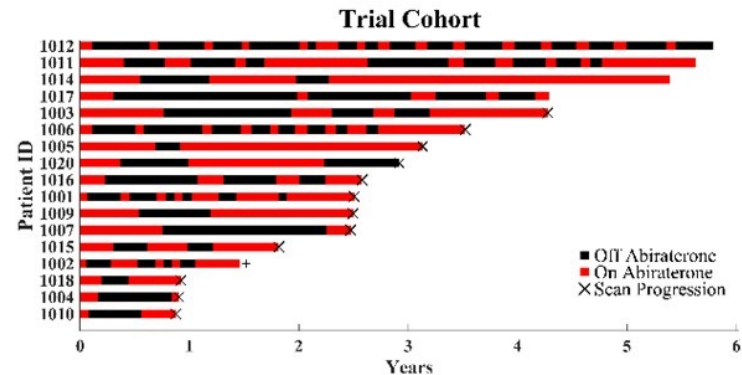
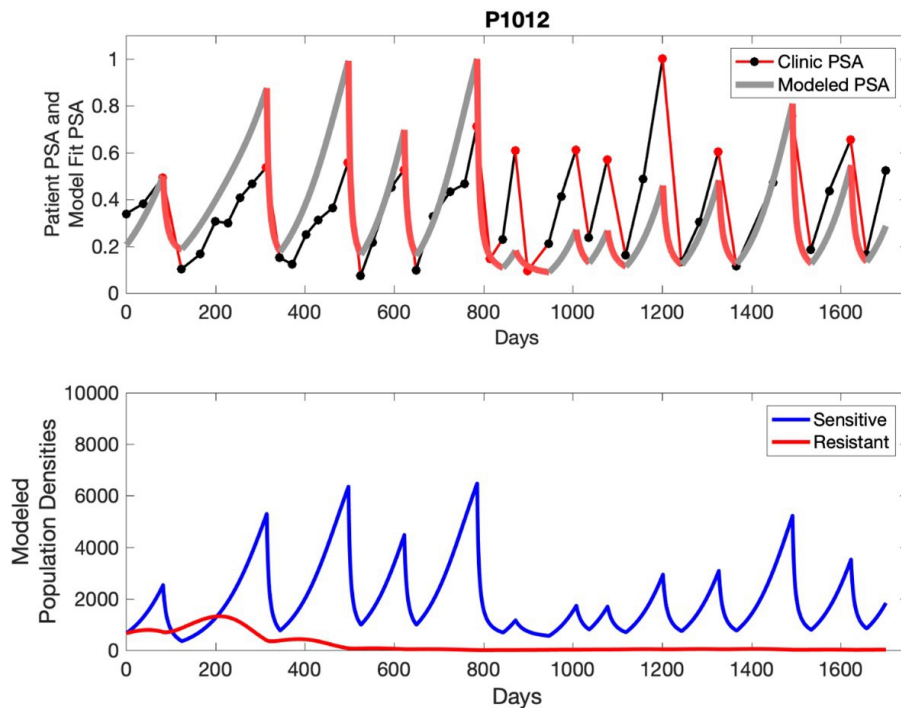
Sponsor ⓘ H. Lee Moffitt Cancer Center and Research Institute

Information provided by ⓘ H. Lee Moffitt Cancer Center and Research Institute (Responsible Party)

Last Update Posted ⓘ 2024-02-21

Would this really work?

Zhang *et al.*, eLife, 2022:



Summary

- >80% of cancer death today are due to therapy failure
- Cancers evolve/change and become resistant
- We can model this process mathematically
- Models help design treatments that keeps cancer **under control**
- The real picture inside a cancer is likely much more complicated



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