– in these contexts, the capacity for the pharmacologically active metabolite Albendazole Sulfoxide to cross the blood-brain barrier and into the cerebral spinal fluid is thought to contribute to the high efficacy of the drug against these parasites17.

* Albendazole a widely used medication for treatment of a variety of parasitic worm infections.
* Historically usage has primarily been in a clinical context where multiple-dose regimen are used to treat infections with parasites such as *E.granulosus* etc.
* Has also found use in programmatic contexts where a single dose is given: this includes programmes treating lymphatic filariasis, and more recently those in contexts where loiasis is endemic, precluding use of other anti-helmintics such as ivermectin and necessitating innovation of current programmatic drug delivery strategies (Test-and-Not-Treat).
* Substantial uncertainty still surrounds the usage of Albendazole and its usage in anti-helmintic treatment. Whilst efficacy has been established for numerous infections, its impact on some of the most public health relevant parasites remains unclear (onchocerciasis, loiasis etc). Perhaps of even greater relevance, it is well established that Albendazole pharmacokinetics display substantial inter (and even intra) individual variability, with profiles of the concentration of the drug’s bioactive metabolite (Albendazole Sulfoxide) in the blood displaying substantial variation in individuals receiving the same dose.
* Whilst numerous reasons for this have been posited in the literature (including pH of the gut and its impact on bioavailability, sex and age-based differences, infection itself), many studies have focussed on only one driver (if at all) and so a systematic understanding of the exact determinants and their comparative impact remains outstanding. A better understanding is important given Albendazole’s ubiquitous usage around the world as an anti-helmintic, and may facilitate dosage regimen that are optimised to the characteristics of the patients being treated.
* Motivated by this, we carried out a systematic review of literature in order to identify references containing temporally disaggregated data of Albendazole Sulfoxide (and Albendazole) concentrations in the blood following treatment. We construct a mathematical model of Albendazole pharmacokinetics that captures key phenomena associated with the drug’s metabolism, including extensive hepatic first-pass metabolism and its typically low bioavailability, amongst others. We fit this model to data collected during the systematic review and use these results to relate key pharmacokinetic properties (drug half-life, AUC, CMax­ ­etc) to characteristics of the patients being treated. In doing so, we provide new insight into the drivers of variation in Albendazole pharmacokinetics and

* Despite widespread usage, much uncertainty surrounds the pharmacokinetics of Albendazole treatment, in particular the drivers of the extensive inter-individual variation observed in individuals receiving treatment. Previous studies have explored individual factors contributing to this variation but a systematic consideration remained outstanding: this is despite the utility such an understanding would have in enabling treatment to be better tailored to patient characteristics.
* Utilising a systematic review and mathematical modelling approach, we explore some of the drivers of this variation, providing insight into their magnitude and effect. Our results reveal the pronounced impact of some of these variables on key pharmacokinetic parameters. Intriguingly, our results indicate that different factors differentially impact different pharmacokinetic properties of Albendazole -more detail here-.
* Additionally, results considered here were restricted to single doses of Albendazole. Whilst this is programmatically the most relevant feature to be considering, use of Albendazole in dedicated medical settings for diseases such as infection with *E.granulosus* often utilise treatment regimen consisting of multiple doses delivered over multiple days. Previous results have shown that Albendazole appears to induce its own metabolism, leading to changes in its pharmacokinetic properties over the course of multiple dose regimen. Exploring this phenomena and its consequence for anti-helmintic treatment would require extension of the mathematical model developed here, and likely represents an instructive avenue of future work.
* There are however, a number of limitations to our analyses. Firstly, because of constraints pertaining to the data available in the literature, we were unable to work with individual patient data, instead having to work with aggregated population level data from many of the references. This limits our capacity to infer individual drivers of variability although doesn’t necessarily preclude our capacity to analyse specific factors (e.g. Sex) where these are known for the entire group. Secondly, data constraints also prevented us examining all the possible factors influencing Albendazole pharmacokinetics – a notable one would be age, with studies having shown the likely existence of age-related differences in Albendazole pharmacokinetics. Irrespective of these constraints however, these analyses allowed us to systematically review many other important factors (Sex, Dose, Infection Status, Other Drugs and Infection Status).
  + Note, consider going back through all the papers and get the mean age data; in which case replace that section with another example of a variable we haven’t been able to assess.
* Also, number of other phenomena not considered here that could be instructive to model – double peak sometimes observed with Albendazole, possible incorporation of a peripheral compartment to reflect the biphasic nature of clearance again, sometimes, rarely observed etc.
* Overall however, and despite these limitations, our work provides insight into the factors governing the variation in Albendazole’s pharmacokinetic variation. More broadly, it provides a framework to optimise treatment regimen based on patient characteristics. Given recent results surrounding the use of Albendazole in innovative programmatic settings (Test-and-Not-Treat), this will likely hold relevance for programmatic settings.