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CARE – Corona Accelerated R&D in Europe

WP3- hits to leads

D3.6 Small Molecule (SM) system impact model - SM system quantitative impact model

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Document History

Version	Date	Description
V1.0	31 Oct 2024	Quantitative impact model of antiviral drug development from early drug discovery to regulatory approval, marketing access and patient receipt, including care seeking, diagnosis and treatment rates. This report includes a detailed description of the model and its main findings as well as potential applications or uses.

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Abstract

This deliverable report presents a comprehensive system dynamics model of antiviral drug development in the context of a public-private consortium responding to a pandemic. The model spans from early drug discovery through to patient treatment, incorporating key subsystems including drug discovery, clinical development, marketing authorization, marketing access, and patient dynamics. Analysis of the model reveals important trade-offs in consortium design and drug development strategy. A fundamental tension exists between consortium size and efficiency - larger consortia benefit from increased innovation potential and collaborative quality improvements but suffer from greater administrative overhead and more complex governance structures. The model demonstrates how resource allocation between priority and backup drug candidates can be optimized under different risk scenarios. It also captures the trade-offs in target product profile (TPP) design, where broader TPPs increase the likelihood of finding effective compounds but may result in lower overall product impact, through having a lower target patient population. Critical system feedbacks are modeled, including how increasing virus understanding reduces pandemic pressure and influences investment decisions, and how market saturation affects the relative benefit of subsequent products. The model serves as a valuable tool for multiple applications: it creates a mechanism for incorporating patient perspectives earlier in drug development, enables optimization of consortium structure for future pandemic response, and supports investment decisions under uncertainty. Its interactive nature allows stakeholders to simulate various scenarios and observe system-wide impacts of local changes, making it particularly valuable for policy makers and consortium designers.

Methods

Data collection

The data used for this research was collected from literature, qualitative interviews and model building sessions with stakeholders from the specified subsystems in the drug development process. All interviews and model building sessions were conducted with either one or two participants at a time. The interviews were approved by the Ethics Committee of UZ/KU Leuven (S66267) and by the Social and Societal Ethics Committee of the KU Leuven University (G-2021-3911).

Regulatory/marketing access

Qualitative interviews conducted with regulatory and marketing access expert in industry, health technology assessment (HTA) bodies and regulatory authorities. The total number of interview participants was n=17. Out of this, 4 are regulatory experts, 2 Health technology assessment bodies, 1 payer organization and 10 experts from industry. The main goal of these interviews was to understand the different regulatory and marketing access practices used during the COVID-19 pandemic and whether these processes could be used in normal times. These interviews were conducted in collaboration with Zilke Claessens, Dr. Liese Barbier and Prof. Dr. Isabelle Huys from the Department of Pharmaceutical and Pharmacological Sciences at KU Leuven. These interviews were conducted between May 2022 and November 2022. Discussions followed a topics guide and lasted approximately 60 minutes. All interviews were conducted in English. These semi-structured interviews were transcribed and processed in NVivo (QSR International, 2024)[1], using thematic framework analysis. Findings from these interviews were incorporated into a system dynamic model in Stella Architect[2]. The model building process was also supplemented by findings form literature publicly available reports, and further reports or supplementary material recommended by interview participants. Follow up validation sessions are still pending with this group of stakeholders.

[1] QSR International. (2024). NVivo (Version [insert version number]) [Computer software]. https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home

[2] Stella Architect, Version 3.7.2, Isee Systems Inc., Lebanon, NH, USA, 2023

Drug development

Qualitative, semi-structured interviews and model building sessions were conducted with experts in drug development and project management within the CARE consortium. The total number of participants was n=11. This included 4 people involved in the project management team of the CARE consortium with a broad high-level overview of the processes occurring in the project. There were 2 experts working specifically on hits-to-leads, 2 experts working on animal models or in vivo screening, 1 expert working in systems biology, 1 expert working in phenotypic screening and 1 expert in clinical trials. The discussions lasted between 60 and 120 minutes. All sessions were conducted in English. Insights were captured during the sessions in a system modelling software (either Miro[3] or Stella Architect[4]) by one interviewer sharing their screen to the other interviewers and participants. The discussions were also recorded and used to further detail the model after the first model building session. Additional validation sessions were held to confirm the model has been built correctly from the initial sessions. The validation sessions lasted approximately 60 minutes and were held in English. All interviews and validation sessions were conducted between June 2021 and August 2022. The aim was first to understand the standard process of drug development, outside of the pandemic context or the context of collaboration within the consortium. Understanding of the standard process and the structuring of this in the model was also supported by findings from literature. Second, we sought to understand what is different in the emergency context resulting from the pandemic as well as the context of the consortium, including what is working well in the consortium and areas where improvements are needed.

Patients

This part of the model was mostly built on findings from literature. Two initial pilot studies were conducted in May 2022 to validate findings from literature and to test the questions and format of the semi structured interviews. The interviews were conducted in English, and followed a topics guide, lasted approximately 60 minutes and were recorded and transcribed using Microsoft Teams' transcription feature (Microsoft Corporation, 2024)[5]. Further patient interviews have not yet been conducted because of low availability of patients. Since no small molecule antiviral treatment was available to treat COVID-19 in the early days of the pandemic, it is not possible to analyse the treatment uptake from the initial the pandemic pressure. However, future research aims to explore patient behaviours in more detail.

System dynamics

Systems thinking is based on the idea that a problem cannot be considered in isolation, but in the full context of everything it could potentially influence (Meadows, 2008). This research uses system dynamics, a simulation modelling technique based on systems thinking, to build a model representing the health system of antiviral treatments. The purpose of building a systems model is to give a full picture of the added value of a particular intervention, including any potential unintended consequences in different parts of the system. System dynamics has been applied to various health system problems such as HIV care and testing (Kok et al., 2015; Weeks et al., 2020), immunization systems (Decouttere et al., 2021) and the US opioid crisis (Jalali et al., 2020; Lim et al., 2022). These examples capture important elements and complexities of the broader health system, such as the social context, the sustainability of the intervention and human behavior. System dynamics was deemed to be the most appropriate methodology for the scope of this research, to be able to capture such additional complexities within the system.

Findings from all described interviews were built into a quantitative model using system dynamics. When analyzing the interviews, the first goal was to understand the basic drug development process. To represent this process, we used stock and flow diagrams. These diagrams are composed of stocks, flows and converters to graphically represent a system and generate behavior. The inflow represents the rate

[3] Miro. (2024). [Online whiteboard and visual collaboration platform]. RealtimeBoard Inc. https://miro.com
[4] Stella Architect, Version 3.7.2, Isee Systems Inc., Lebanon, NH, USA, 2023
[5] Microsoft Corporation. (2024). Microsoft Teams [Computer software]. https://www.microsoft.com/microsoft-teams

at which the stock increases and the outflow represents the rate at which the stock decreases. The rates of change can be impacted by any other variable in the system, both converters and stocks (Sterman, 2000). 'Converters' are the additional variable that contribute to the rates of change of stocks. Once all the relevant variables were identified we could identify the relevant connections, dependencies and feedbacks. This made the important dynamics and tradeoffs in the system clear. We analyze and compare these effects and dynamics across the different sub systems.

Results

Using interviews and data collected we build a quantitative system dynamics model of the health system surrounding antiviral development and delivery including the following sub systems: drug discovery, repurposing, hits to leads, clinical development, marketing authorisation, market access, patient antiviral market, budget allocation, virus learning and consortium dynamics. These subsystems are further detailed in this section.

Drug discovery subsystem (WP1&WP2)
The drug discovery subsystem models the work done in WP1 and WP2, target-based and phenotypic drug discovery. The processes of phenotypic and target-based drug discovery are modelled using stocks and flows. The model represents the progression of molecules or compounds from an initial library of compounds to hit compounds that are selected to be progressed to WP3 hit to lead development.

Assay development process
The first step in the process modelled is the design of assays. This is modelled with stocks for both the phenotypic and target-based streams. The inflow to the stock of phenotypic high throughput screening assays is determined by the average assay development time, average cost to develop assays, the money spent on assay development and whether there are existing assays available for that indication. If there are existing assays, the new assays will be developed faster, if there are no existing assays or few existing assays, the new assays will take longer to develop, this is modelled as an increasing concave function. This effect was reported in interviews, that designing new assays for the new coronavirus made the startup time for the drug development process relatively longer.

Similarly, there is a stock of target-based assays that works in a similar way, but there is an additional stock of potential drug targets that influences the inflow to the stock of target-based assays. The inflow to the stock of potential drug targets is also determined by costs, spending and whether targets have already been developed. This has the same effect that if there are no known targets then the process of identifying the first target is harder or slower and if there are known targets, identifying new targets becomes easier and faster, but this increase reaches a maximum, since new targets can't be identified infinitely, so this is modelled with a concave function. The inflow to the stock of target-based assays is based on costs, average time to develop, whether there are existing assays, the number of targets that have been identified or selected to be used within the consortium and the average number of assays developed per target. Based on stakeholder discussions we assume a maximum number of potential targets and potential assays that can be developed, and we assume that the next parts of the system, specifically the screening process doesn't start until these stocks have started tending towards the maximum level.

Compound selection and screening
After the stock of targets and the stocks of assays are full, the next part of the process can begin. The main pipeline of this subsystem is the progression of molecules or compounds through stocks and flows. This starts with a stock of compounds libraries; this stock represents all the libraries from all of the consortium partners. First, compounds are selected for screening, so the two outflows from this stock are

an outflow of compounds selected for phenotypic and compounds selected for target-based screening. These outflows are based on the cost of selection, the resources spent, the max potential selections and the average selection time.The max potential target-based selections is a function of the stock of potential drug targets (we assume, there is an upper limit to potential selections to simplify the process for modelling purposes, and we validated this concept in stakeholder discussions). These outflows are the inflows to the stock of compounds selected for phenotypic or target-based screening. The compounds then flow from the stocks of compounds selected for screening to the stock of screened compounds (this happens in parallel for target based and phenotypic). The flow between compounds selected and compounds screened is determined by the average cost, average time, resources spent and the stock of assays that were developed.

From the stocks of screened compounds, there are two outflows; compounds are either rejected or identified as potential hits. These outflows are determined by assay quality, the exogenous unknown number of effective compounds, the TPP, the average cost, resources spent and the average time for this process. Assay quality is modelled as a stock, that tends towards (but never reaches) 1, or 100% effectiveness in identifying the unknown exogenous number of hits. The inflows to this stock are an average rate learning over time, and the added value of collaboration from the consortium. This added value from the consortium can be interpreted as the added quality in terms of assay design, interpreting the results or any other discussion with other consortium members about this part of the process. This benefit increases over time as trust and familiarity between partners increases. The exogenous number of effective compounds is modelled using a random function because it is unknown. The random function means this number varies for each time the model is run, this is useful for exploring different scenarios. The TPP is modelled as a percentage, to represent that the target product can be defined as being more broad or narrow, the more specific or narrow the TPP, the smaller the percentage, and the more generic, the higher the percentage.

The outflow to the stock of potential hits then works as follows: there is a unknown exogenous number of compounds from the initial library that are actually effective, this cannot be known, but we get evidence or indication of this number from the assays or tests that are run, so a percentage of this exogenous unknown number is the number of compounds actually identified as effective, this is determined by the stock of assay quality, which tends towards 1, or 100%, but doesn't reach this, because it would be unreasonable to assume that all possible effective compounds are perfectly identified. Then a fraction of these compounds is selected to progress based on the TPP. There were also instances of the TPP changing due to assay results, this is shown in the model. The outflow of rejected compounds is similarly determined by assay quality, exogenous effective compounds, TPP, time, cost and resources spent. The identification and rejection rates are determined in the same way for the target based and phenotypic pipelines. So, the identification rates lead to a stock of hits from phenotypic drug discovery and a stock of hits from target based drug discovery. There is an additional delay as this point, we model that the compounds do not flow out of these stocks to the hits to leads sub system until they are formally approved. We model that these can only be approved at a monthly meeting (e.g. SCOM) this means that the identified compounds can be waiting in the stock of hits until the next monthly meeting before they can progress. This part of the model can be used to show the overall impact on the system of these governance delays and can be used to simulate different ways of consortium organization.

Hits to leads subsystem (WP3)

This then continues to the next sub system, the hits to leads sub system, which models the work done in WP3. Similarly to the previous sub system, this process starts with the design of experiments, in this case is the design of screening cascades. We include a stock of screening cascades for the hits to leads stage and a separate stock for the screening cascade at the lead optimisation phase. This process is more standardised and is mainly determined by the costs, resources spent, and average time needed, but this also links to another subsystem, the WP6 animal models subsystem. In this subsystem, in vitro models and animal models are designed and tested, and then become important parts of the screening cascades

designed for WP3.

Animal and in vitro model design (WP6)
The process of designing and testing these models is as follows: models are designed for validation, the inflow to this is based on costs, time and whether there are existing models for that indication. This work in the same way as the inflow to the stocks of assays in the drug discovery subsystem. The models are then validated so there is an outflow for validated and rejected models. These outflows are determined by average costs, time and average success rate, and there is an additional delay for material availability. We model that when pandemic pressure is high and there are many different companies and research centres working on a particular drug indication, the availability of materials for this development will be lower, this could be specific animals needed or any other material used. So based on these variables and this delay, a stock of validated models is identified.

These are then approved to be included in WP3 screening cascades with a monthly meeting delay variable. This same process of model design and validation is included in the model for in vitro models (IV), small animal models (SA) and large animal models (LA). All types of models or tests in WP6 are divided and aggregated across these three categories. Where the validated and approved in vitro models impacts the inflow to the stock of hit to lead screening cascades, and the stock of small and large validated and approved animal models influences the inflow to the stock of lead optimisation assay cascades.

Analogue synthesis and screening
Similarly to the drug discovery subsystem the main hits to leads processes don't start until the screening cascade stock is 'full'. This is we assume for the simplicity of modelling, it adds a lot of complexity to the model to have these processes running in parallel, so for simplicity we keep it sequential. The hits identified from target based and phenotypic drug discovery enter the WP3 hits to leads subsystem. The first step we model is an initial 'hit explosion', where hit analogues are synthesised for every hit. There is an inflow to a stock of analogues, which is determined by the number of hits identified, the average number of analogues needed per hit and the average cost and time of synthesising new compounds. This stock of analogues is screened or tested using the assay cascade designed. The flow from the stock of analogues to the stock of screened analogues is therefore determined by the screening cascades stock, the average cost, average time, resources spent and screening capacity.

After one round of screening, no compounds in the stock of screened analogues are identified as effective, new analogues are synthesised based on the most effective compounds screened and then the new analogues are tested through the screening cascade again. This is represented in the model by an outflow from the stock of screened analogues, this outflow influences another inflow back into the stock of analogues. The analogue synthesis rate is based on the number of screened effective compounds selected for resynthesis, the average cost, time and resources spent, and the average number of analogues needed per compound. The average number of analogues per compound is a decreasing function of the number of iterations of the rounds of synthesis and screening and is also influenced by random variance. This random variable in included because there is some level of risk or uncertainty in the creation of new compounds to optimise the compound to meet all characteristics of the TPP. Compounds or analogues cycle through these stocks of analogues and screened analogues through multiple rounds of iteration.

Evidence generation process

As all compounds or analogues are screened and through each iteration of this there is an accumulation of evidence about the effectiveness of the compounds. This is modelled with a stock of evidence. The

inflow to the stock of evidence is determined by the total number of screens and re screens that take place, specific the flow from analogues to screened analogues impacts the inflow to evidence generated. Then the inflow to evidence generated is also influenced by assay quality, random variance in evidence generation, and the unknown exogenous percentage of actually effective compounds. Assay quality is measured as a stock, similar to the assay quality in the drug discovery sub system, the inflow to this stock is also based on an average learning rate over time, and the additional collaboration benefit from being a part of a consortium, which can be interpreted as improved assay design, results interpretation etc. We add an additional variable for random evidence variance, to show that evidence generation isn't perfect and only a fraction of the true effective compounds can be successfully identified as effective through research. This level of precision of evidence generation is to some extent unknown, because the true number of effective compounds is unknown, so this variance in the evidence is also modelled with a random function. The actual unknown exogenous number of effective compounds is modelled in a similar way as in the drug discovery subsystem, but now the fraction of screened compounds that are actually effective is increasing with the number of iterations of synthesis that occur, because with each round of synthesis, more is understood about the compounds and the process of synthesising becomes more targeted and focused. Therefore, the process of evidence generation is as follows: a certain percentage of all screened compounds is actually effective and a fraction of the actually effective compounds accumulates evidence of effectiveness based on assay quality and a random evidence variance factor.

The stock of evidence is then what determines the acceptance or rejection of screened analogues. If the evidence generated is above a certain evidence threshold, then the compounds will be accepted and if they are below, the compounds will be rejected. The evidence threshold is also based on the TPP percentage. If the percentage is higher, then more compounds will be accepted and if the percentage is lower, then less will be accepted. This can be interpreted as, if the TPP is more broad and easy to fit, more compounds will be accepted and if the TPP is more narrow and selective, then less will be accepted. So, in this case a more broad spectrum TPP would actually be a narrower or lower percentage than a TPP that can be effective against any one strain, that is, meeting one specific strain is in some ways easier than meeting many specific strains, or being more broad spectrum. The harder the TPP criterion are to meet, the lower this TPP selectivity percentage is. The compound acceptance rate is additionally influenced by average time to interpret the evidence, average cost of evaluation and resources spent. Then when effective compounds are identified based on evidence and TPP, there is an additional delay for them to be formally approved and to move to the next phase, in this case it's a monthly meeting delay, an effective compound has to wait until the next monthly meeting to be formally approved to the next phase.

This iterative process of analogue synthesis, screening, evidence generation and approval is the same for lead optimisation as hits to leads, so this exact process repeats for hits to leads and then lead optimisation, however with different values, where the approval from the hits to leads phase leads to lead optimisation and the approval from lead optimisation leads to candidate for clinical trials. Additionally, in this subsystem we model the relative resources spent on priority and backup series. A larger portion of the resources and spent on a smaller number of the series or assets. This is a way to mitigate the high risk of drug discovery. this risk is included in the model using random variation at various points in the process. These two parts of the model can be used to simulate the optimal balance between spending resources of priority and backup, as well as the fraction of resources to prioritise, in different levels of risk or uncertainty.

Clinical Development Subsystem (WP8)

The approved compounds that have been screened through the lead optimisation process are then candidates for clinical development, this leads us to the clinical development subsystem which models the work done in WP8 of CARE, but additionally all other antiviral products that reach clinical trials are included in the model from this point on.

Clinical Trial Progression

This subsystem models how all products progress through a stock of phase 1, phase 2 and phase 3 clinical trials, and how each product accumulates safety and efficacy evidence for each time unit the product is in each phase of clinical trials. When a product enters the stock of phase 1 clinical trials in the model, there is an accumulation of safety evidence for each time unit the product is in the stock of clinical trials. This is measured as a stock of safety evidence. We assume that evidence generation accumulates as an S-shaped function because early in the trial, the evidence accumulates slowly at first as patients are enrolled and initial responses are observed, in the middle of the trial as more data becomes available and more patients progress through treatment, evidence accumulates more quickly, reaching a rapid growth phase, and at the end of the trial, evidence accumulation tends to plateau as the trial nears completion. By this time, most patients have completed the protocol, and only marginal new information is being added. Additionally, this S-shaped function is increased with some random variance, due to uncertainty. If the evidence generated in the stock of safety evidence in above a certain safety evidence threshold after the minimum trial time, then the product is approved to move to the stock of phase 2 clinical trials, if the stock of safety evidence is lower than this threshold after the maximum trial time, then the product is rejected and does not progress.

The evidence generation works similarly in phase 2 trials, safety evidence accumulates in the same stock of safety evidence for each product and follows a similar S-shaped growth with random variance, but additional efficacy evidence is generated, so there is an inflow to an additional efficacy evidence stock. This evidence accumulation also follows S-shaped growth with random variance for the same reasoning as previous. Similarly, if the safety and efficacy evidence is above a threshold after the minimum phase 2 trial time, the product will be approved for phase 3, and if either threshold is not met before the maximum trial time, then the product will be rejected and not progress to the next phase of clinical trial. This process repeats for phase 3 trials, but with different magnitudes, and the products that are approved to continue after phase 3 trials are then candidates for marketing authorization.

Marketing Authorization Subsystem

The marketing authorisation subsystem has two streams, the conditional marketing authorisation and the normal marketing authorisation stream. The approval for either stream is based on the stocks of safety and efficacy evidence that are accumulated in the clinical development subsystem.

Normal marketing authorisation

For the normal approval stream there is a stock of products in the authorisation process, the inflow to this is based on the stocks of safety and efficacy evidence, the threshold for safety and efficacy needed for approval and the number of candidates that have completed clinical trials. After an average review time, typically 12 months, the product is either accepted or rejected. This average time is faster during the pandemic when pandemic pressure is high, because of additional mechanisms like the rolling review or emergency task force. So, when pandemic pressure is higher, this approval process goes a lot faster, up to twice the regular speed, and when pandemic pressure has eased off the process returns to the normal longer speed. The authorisation and rejection rates are also determined by an average approval rate with random variance. Based on historic data, this average approval rate is also higher when pandemic pressure is higher. The process is modelled in this way because there is some uncertainty in the approval process. Companies submit their product for approval when they think their product has sufficiently met the evidence thresholds, but not all products that apply for approval get accepted, this is why the evidence generated and thresholds are modelled at the submission phase and the average approval rate and time is what determines the progression from the stock of products that have been submitted and the stock of products with full approval.

Conditional marketing authorisation
The process works similarly for the conditional authorisation process, but the evidence thresholds are lower and the products can be submitted for approval before they finish phase 3 clinical trials. The average review time is also shorter and is additionally accelerated in the same way by the pandemic actions that are motivated by pandemic pressure. After products have been conditionally approved, they have one year to meet the normal safety and efficacy thresholds, if the required safety and efficacy is not approved in this time, the products authorisation is revoked. Additional time is taken to review the conditional approval for full approval. Though the products reach the market quicker, many stakeholders reported that the overall process of conditional approval takes more time and resources, because the review process has to happen twice. This model can be used to simulate the conditions under which this extra use of resources is justified.

Market Access Subsystem
The stock of products with conditional marketing authorisation or full marketing authorization are then candidates for market access. All candidates with marketing authorisation go to the market access subsystem and enter the stock of products in the market access process.

HTA assessment and price negotiations
The first step of this is a HTA assessment, all products undergo a HTA assessment, this takes a standard amount of time, this process goes faster in a pandemic but requires a lot more resources to be spent because in the context of the pandemic there are many more products to review. After the HTA assessment, products enter the stock of products in pricing and reimbursement negotiations. From this, products are either accepted or rejected based on an average negotiation time and an approval rate. The approval rate is determined by the qualities of the product relative to all other products available on the market. The safety and efficacy evidence accumulated is considered relative to the safety and efficacy profile of the products that have already been approved, and the cost of the product is considered relative to the cost of the product already on the market. The HTA authority will agree to a pricing and reimbursement plan if there is some relative benefit in terms of safety, efficacy or cost effectiveness (the scope of this research is Europe, in reality these assessments are done by each national HTA organisation separately, but for modelling purposes we aggregate this process across the European market). An improvement in safety can be interpreted as less side effects or the potential to treat an additional patient population.

There is an additional inflow to the stock of drugs with market access, a pandemic fast track. This was particularly seen for vaccines early in the pandemic, that governments bought vaccines and agreed on pricing and reimbursement plans even before the clinical trials were finished for these products, therefore a HTA assessment could not properly be conducted for these products. This was mostly the case for vaccines during the pandemic, but it is also a potential pandemic mechanism for antivirals, this is why we include it in the model for scenario simulation. The products with marketing authorisation and market access are then available to the patient population.

Patient Subsystem
This leads to the patient subsystem, which is modelled building on a standard SIR structure (Kermack & McKendrick, 1991). Our model starts with a stock of the susceptible population, this has two standard inflows and outflows that are always there, even outside of a pandemic, a standard birth rate and death rate.

Infection rate
The main outflow for this model is the outflow to the stock of unknown infected, this outflow is determined by the infection rate. The infection rate is determined by the infectiousness of the virus as well as additional measure that limit the spread of the virus. In this model we include the impact of social

distancing, so lower infection rate people because of less contact; and the impact of a vaccine being available, so lower infection rate because of higher immunity. We keep the values for social distancing and vaccination rates fixed in all scenarios and calibrate to real data in the base case. From the stock of unknown infected there are three outflows, an outflow to the stock of unknown infected recovered, untreated undiagnosed deaths and to the stock of diagnosed. The flow from unknown infected to diagnosed is determined by the diagnosis rate. The diagnosis rate is determined by care seeking and the availability of diagnostics. Care seeking is influences by the level of pandemic pressure or fear of the virus and public understanding of the virus. Those who are not diagnosed will either naturally recover or die, based on the mortality rate, average mortality time and average recovery time. From the stock of unknown infected recovered, people will return to the susceptible population later, based on the duration of the immunity.

Treatment Rates and Outcomes

The stock of diagnosed people similarly has three outflows, the outflow to the stock of untreated diagnosed deaths, untreated diagnosed recovered and the stock of treated. The outflow to the stock of treated is determined by the treatment rate. The treatment rate is determined by the treatment demand, the time of diagnosis, and whether there is a product available. If there is no treatment available the treatment rate must be zero, and for any number of treatments available greater than 1, the treatment rate can be positive. The number of treatments available is determined in previous subsystems. If the time of diagnosis is too long after the time of entering the stock of unknown infected, then the treatment rate will also be zero, in our base case we model a 48-hour treatment window. If there is a treatment available and the patient has been diagnosed within 24 hours of being infected, then the treatment rate will be determined by the treatment demand.

The treatment demand is determined by the level of safety and efficacy evidence accumulated about the product, which is accumulated in the clinical development subsystem, the price the patient has to pay for the product, and the patients safety threshold, price threshold and efficacy threshold. These values are calibrated to match historic data for treatment rates, but future research will further investigate the relative importance of these treatment attributes for patients. Those who are not treated will either naturally recover or die, this is determined by the mortality rate and average recovery times. The people in the stock of untreated undiagnosed recovered will eventually re-enter the stock of susceptible population based on the natural immunity duration. Those who enter the stock of treated people will flow to recovered or dead. This is determined by the actual safety and efficacy rate of the drug. Those in the stock of treated recovered will eventually re-enter the stock of susceptible population, based on the treated immunity duration, which is a function of the natural immunity duration and the treatment efficacy, the idea being that the more effective the treatment the longer the immunity.

System Feedbacks

This subsystem can be used to simulate and show the main downstream impact of the consortium, in terms of how many patients can benefit from the treatment and the added value to patients of a CARE product if there already existing approved products available. This subsystem also highlights all the potential limiting factors to a patient receiving treatment, such as slow care seeking or patient beliefs. This also identifies potential mechanisms through which higher patient treatment uptake could be promoted.

Unmet medical need

The number of cases and deaths modelled in the patient subsystem also influences and feeds back to various other parts of the system. The number of cases, deaths and treatments available determines the level of unmet medical need. When there is no treatment available unmet medical need is high. As soon as one product becomes available, unmet medical need drastically decreases, then slowly decreases and more and more products become available and more, smaller patient subgroups get access. The idea is that because of side effects and contra indications, not all patients will be able to take the first treatment

available, so as additional treatments become available with different safety profiles, more patients can potentially find a treatment available, but most of the medical need of most of the population is met as soon as one treatment is available. So unmet medical need is a convex decreasing function of products available.

Pandemic pressure
Further pandemic pressure is a function of cases and deaths, as well as understanding of the virus. Deaths and cases are weighted against expected cases and deaths, so earlier in the pandemic which the high number of cases and deaths was more of a surprise, pandemic pressure was higher, but later in the pandemic, when cases were still high, but the virus was more known and understood, there was lower pandemic pressure for the same level of cases. The number of deaths is also weighted higher than cases, so if cases are still high, but deaths are lower, then pandemic pressure will be much lower. Pandemic pressure also increases with knowledge or understanding of the virus, early in the pandemic the virus is unknown and it is unknown how possible or quick it will be to find a solution. This fear of the unknown contributes to pandemic pressure. Later, even if there is no product yet available, just having some products in the pipeline and the virus generally better researched and understood will contribute to a lowering of pandemic pressure. Because of these factors, pandemic pressure in our model is simulated to be at its highest in the first year or so of the pandemic and much lower afterwards.

Impact on System Components
This stock of pandemic pressure included in the model influences various other parts of the model. This is the key determinant of the pandemic or emergency investment decisions, and the reason there was so many vaccine and drug development initiatives started in the first year of the pandemic, and similarly the willingness to invest also greatly depleted later into the pandemic. The model includes standard spending, investment and payoff rates for industry and public resources and models the shift in both public and private resources towards pandemic initiatives in response to the pandemic pressure. The pandemic pressure also influenced the willingness to work and contributes to many standard processes running a lot faster earlier in the pandemic relative to normal timelines, particularly market access and approval timelines.

This high pandemic pressure and high unmet medical need influenced the budget allocation to the CARE project, the willingness for many public private partners to collaborate in the context of a consortium, and the speed at which the project was designed, agreed and approved. The design of the product proposal was also influenced by a very high willingness to work based on a high pandemic pressure.

Additional Subsystems
Some additional subsystems included in the model, but not discussed in detail are the repurposing stream, HR dynamics, virus understanding and budget allocation.

Repurposing
The repurposing subsystem uses the same concepts and mechanisms explained for the drug discovery and hits to leads subsystems, but is a simplified and shorter process because it starts from a stock of drugs, instead of a stock of compounds that need to be developed into a drug candidate.

HR dynamics
The HR dynamics subsystem models the number of partners in the consortium and the associated governance structure of the consortium. This includes the frequency of each type of meeting, and the relevant bodies needed to approve each decision. For example, we discussed the hits approved in the drug discovery subsystem are delayed because they wait for the next monthly meeting for formal approval. Which decision needs to be made at which meeting and the frequency of each of these meetings is modelled in this subsystem. Further the frequency of meetings, and the number of approval points increases as the number of consortium members increases i.e. the consortium structure gets more

convoluted as the consortium gets bigger.

Additionally, in this subsystem we model the average time spent per partner on meetings or reporting, or time spent on generic administrative tasks that is not spent on hard science of the progression of the candidates through the main model pipeline. In our model we show this delay on non-science tasks to be an increasing function of consortium partners, i.e. the larger the consortium, the more administrative delays there are and the smaller, the more streamlined these processes are. The benefit of more partners is the impact on quality, which was discussed to be included at various points in the consortium pipeline. This impact of collaboration on quality is modelled as a stock and is described by a concavely increasing function of consortium members. This subsystem can be used to simulate scenarios for different consortium sizes.

Virus learning and budget allocation
The virus learning sub systems shows that understanding of the virus increases as more research is done, which decreases pandemic pressure. And the budget allocation sub system shows how money is divided across the different work packages of the consortium and the portion of budget allocated as a reserve. This can be used to simulate scenarios for different consortium budget allocation.

Discussion

The system dynamics model of antiviral drug development through public-private consortiums reveals several fundamental tradeoffs and feedback mechanisms that shape system performance. Through simulation experiments using mock data, we investigated how varying parameters in different subsystems impacts outcomes across the entire model, enabling identification of key system interactions. Three critical tradeoffs emerged: the consortium size tradeoff between collaborative benefits and coordination complexity; the resource allocation tradeoff between prioritizing promising candidates versus maintaining backup options; and the target product profile tradeoff between broader patient benefit and development complexity. The model also captured two essential feedback loops: virus dynamics, where pathogen evolution and spread influence development priorities and pandemic pressure; and market saturation feedbacks, where existing treatment availability affects both development incentives and unmet medical need. While final data from consortium partners is still being collected, these preliminary simulations demonstrate the interconnected nature of the system and highlight critical relationships between variables. Future work with complete empirical data will quantify the specific magnitudes of these system effects, but the structural insights about core tradeoffs and feedbacks provide valuable guidance for consortium design and management. This analysis explores how these interrelated dynamics impact system behavior and outcomes.

Tradeoffs
The model captures several fundamental trade-offs that emerged from stakeholder interviews as critical considerations in collaborative antiviral drug development. Three key trade-offs are particularly significant and are explicitly represented in various components of the model. First, there is a crucial organizational trade-off regarding consortium size, balancing the enhanced innovation potential of a larger partnership against increased administrative complexity and coordination challenges. Second, the model addresses the strategic resource allocation dilemma between prioritizing resources on promising lead series versus maintaining development of backup candidates to mitigate risk. Third, there is an important tension between Target Product Profile (TPP) breadth and patient benefit, where easier development pathways enabled by broader TPPs must be weighed against the potentially greater therapeutic value of more targeted approaches. The following sections detail how these trade-offs are represented in the model structure and how the model can be used to simulate different scenarios to

explore optimal approaches under various conditions.

Size trade-off
The model captures a fundamental trade-off in consortium size that emerged from stakeholder interviews: while larger consortiums can potentially drive greater innovation through diverse expertise and collaboration, they also introduce significant operational complexity and administrative overhead. This trade-off is explicitly modelled through two competing mechanisms: quality improvements that scale with consortium size, and administrative delays that increase as more partners join.

The quality benefits of a larger consortium are represented in the model as an increasing function of the number of partners, reflecting how diverse expertise and collaborative learning can enhance key processes throughout the drug development pipeline. This improvement manifests in various ways, from better assay design and interpretation to more robust screening processes. However, this benefit shows diminishing returns, modelled as a concave function - while adding initial partners may substantially boost innovation potential, the marginal benefit decreases as the consortium grows larger. This aligns with interview insights suggesting that while diversity of expertise is valuable, there comes a point where additional partners add less unique value.

Counterbalancing these benefits, the model captures how larger consortiums introduce increased administrative burden and coordination challenges. This is implemented as an increasing function of consortium size affecting meeting frequency, reporting requirements, and approval delays. For instance, the model shows how compounds identified as hits must wait for monthly steering committee meetings for formal approval before progressing to the next development phase - a delay that becomes more significant as the consortium grows and governance structures become more complex. Interview data suggested that in larger consortiums, scientists spend proportionally more time on administrative tasks rather than core research activities, a dynamic captured in the model through increasing delays in non-scientific tasks as partner numbers grow.

These competing mechanisms create an implicit optimal consortium size that balances innovation potential against operational efficiency. In smaller consortiums, processes are more streamlined with fewer approval gates and less coordination overhead, allowing for faster progression through development stages. However, they may miss out on valuable cross-pollination of ideas and expertise that could improve drug candidate quality. The model allows exploration of this trade-off through scenario analysis, helping to identify consortium structures that maximize the benefits of collaboration while minimizing administrative friction.

Prioritisation trade-off
Another key trade-off captured by the model is the allocation of resources between priority and backup series. This trade-off emerged consistently in stakeholder interviews as a fundamental approach to managing the inherent uncertainty of drug discovery. The model explicitly represents how resources are divided across multiple drug candidates, with a larger portion of resources typically allocated to priority series and smaller portions to backup candidates.

The key tension in this resource allocation decision lies in balancing risk against development speed. One approach is to spread resources more evenly across many series, allocating significant resources to multiple backup candidates. This strategy provides a safety net against failure - if one series proves unsuccessful, other viable candidates remain in development. However, this risk-mitigation approach comes at the cost of slower overall progress, as resources are divided among many parallel efforts rather than concentrated on driving rapid advancement of the most promising candidates.

The alternative strategy is to heavily prioritize resources toward a small number of lead series. This concentrated investment can accelerate development of priority candidates, potentially bringing successful drugs to market faster. However, this approach carries substantially higher risk - if the prioritized series fail, a significant portion of invested resources are effectively lost with no backup candidates sufficiently advanced to quickly take their place. This risk is particularly pertinent given the high uncertainty inherent in drug discovery, where promising candidates can fail for numerous unforeseen reasons even in late stages of development.

The model enables exploration of optimal resource allocation strategies through scenario analysis incorporating different levels of risk and uncertainty. By simulating various resource distribution scenarios - from highly concentrated to broadly distributed allocations - while varying risk parameters, the model can help identify resource allocation strategies that best balance development speed against risk mitigation for different risk profiles. This capability allows investigation of questions such as what portion of resources should be prioritized to lead series versus maintained for backups, and how this balance should shift under different levels of development risk or uncertainty.

TPP trade-off

The model incorporates a key strategic trade-off regarding the breadth of the Target Product Profile (TPP), which influences multiple stages of the drug development pipeline. The TPP is represented as a percentage parameter that captures how selective or how broad the target characteristics are, with significant downstream implications for both development complexity and ultimate patient benefit.

In the drug discovery subsystem, the TPP percentage directly influences the rate at which compounds are identified as potential hits. A broader TPP (represented by a higher percentage) means more compounds will be accepted as potential hits, as they need to meet less stringent criteria. This is modelled in both the phenotypic and target-based screening processes, where the outflow to the stock of potential hits is partially determined by the TPP percentage. The model shows how a broader TPP leads to higher hit identification rates, potentially accelerating the early stages of drug development.

This effect continues through the hits-to-leads and lead optimization phases, where the TPP percentage influences the evidence thresholds for compound progression. The model captures this through the relationship between the TPP and the acceptance/rejection rates of screened analogues. In the iterative process of analogue synthesis and screening, compounds are accepted when the accumulated evidence exceeds an evidence threshold that is calibrated to the TPP percentage. A broader TPP means a lower evidence threshold, resulting in more compounds progressing through these development stages.

However, the model also captures the downstream implications of TPP breadth in the patient sub-system, creating a crucial trade-off. While a broader TPP may facilitate easier drug development, it results in products with more limited therapeutic value. This is reflected in the treatment demand calculations within the patient sub-system, where treatment uptake is influenced by the product's efficacy profile. The model shows how a narrower, more targeted TPP - while making drug development more challenging - can lead to products that better meet specific patient needs and potentially achieve higher treatment rates among their target population.

The model enables simulation of different TPP strategies to explore this fundamental tension between development feasibility and therapeutic value. By running scenarios with varying TPP percentages, it becomes possible to evaluate how different approaches to TPP definition influence both development success rates and ultimate patient benefit. This can help inform decisions about optimal TPP definition, particularly in contexts where there may be pressure to pursue broader, potentially easier-to-develop products versus more targeted therapies that could provide greater patient value but face higher development hurdles.

Feedbacks

The system dynamics model captures several important feedback loops that influence antiviral drug development trajectories. Two particularly significant feedback mechanisms emerge from the model structure and stakeholder interviews. First, there is the relationship between virus novelty and innovation dynamics: when a virus is new and unknown, pandemic pressure drives high incentives for treatment development, while simultaneously the lack of existing research makes innovation more challenging. As understanding increases, innovation becomes easier, but incentives decrease. Second, there is the feedback between market availability and development dynamics: the absence of available treatments creates high unmet medical need driving development, while successful market entry both reduces this need and increases knowledge that facilitates further development. These feedback loops create complex dynamics that influence the progression of antiviral drug development. The following sections examine these feedback mechanisms in detail, exploring how they manifest in the model and their implications for drug development strategy.

Virus understanding feedback

The model captures a critical feedback loop in virus dynamics that emerged from stakeholder interviews: the inverse relationship between virus novelty and innovation capability, balanced against innovation incentives. When a new virus emerges, there is an immediate surge in the incentive to develop treatments and countermeasures, but paradoxically, this is precisely when innovation is most challenging.

This dynamic manifests through several interconnected pathways in the model. When a virus is new and poorly understood, there is typically no existing treatment available and limited understanding of potential countermeasures. This creates significant pandemic pressure, which drives increased investment and willingness to work on developing treatments. The model represents this through the "pandemic pressure" stock, which rises sharply with new virus emergence and influences both public and private resource allocation toward drug development initiatives. This was evident in stakeholder interviews, where participants described an unprecedented mobilization of resources and urgency to develop treatments early in the pandemic.

However, this same novelty that drives innovation incentives also creates substantial barriers to actual drug development. The model captures this through several mechanisms: First, the lack of existing research on potential drug targets means the "stock of potential drug targets" starts nearly empty and fills more slowly due to limited foundational knowledge. Similarly, the development of both phenotypic and target-based assays is hindered by the absence of existing assays to build upon. This was highlighted in interviews where stakeholders described the significant challenges in designing new assays for the novel coronavirus, leading to longer startup times for drug development processes.

The model further represents this challenge through the animal model development subsystem, where the creation and validation of new models takes longer when there is no existing research foundation. Additionally, the probability of finding effective compounds, whether through new synthesis or drug repurposing, is lower when dealing with a novel virus due to limited understanding of its mechanisms and potential vulnerabilities. This is captured in the model through lower initial hit rates and higher rejection rates in both the drug discovery and repurposing pipelines.

As virus understanding increases over time (represented by the "virus learning" subsystem), these innovation barriers gradually decrease. The model shows how accumulated knowledge leads to faster assay development, more efficient target identification, and improved screening processes. However, this improvement in innovation capability is ironically accompanied by declining innovation incentives, as pandemic pressure decreases with greater virus understanding and the potential availability of initial treatments. This creates a complex temporal dynamic where the peak of innovation capability often occurs after the peak of innovation incentive has passed.

This feedback loop highlights a fundamental challenge in pandemic preparedness: the need to maintain innovation capabilities and research foundations during non-pandemic periods, so that when a new virus emerges, the technical barriers to innovation are lower despite the virus's novelty. The model can be used to simulate different scenarios of preparedness investment and its impact on the speed and effectiveness of response to new viral threats.

Market saturation feedback

The model also incorporates important feedback dynamics between market availability, unmet medical need, and drug development incentives that were identified both through stakeholder interviews and literature review. These dynamics create a self-regulating system where the absence of available treatments simultaneously creates both opportunities and challenges for drug development.

When no treatments are available for a virus, the model represents this through high unmet medical need, which creates strong market incentives for drug development. This high unmet need translates into potential profit opportunities, as successful treatments would address a completely unserved market. However, this same absence of existing treatments also means there is limited knowledge about effective therapeutic approaches, translating to higher development risks. The model captures this through lower initial success probabilities in the drug discovery and clinical development phases when no previous treatments exist.

As the first successful treatments reach the market, the model shows how this triggers several interconnected feedback loops. First, unmet medical need begins to decrease substantially with the availability of the first treatment, represented as an exponentially decreasing function of available products. This initial sharp decrease in unmet need reflects that the first available treatment addresses the basic therapeutic need for the majority of the patient population. However, the model also captures how some level of unmet need persists even after initial market entry, representing patient subgroups that may not respond to or tolerate the first available treatment due to contraindications or side effects.

Simultaneously, the successful development and market entry of initial treatments increases the overall knowledge base about treating the virus. The model represents this through the "virus understanding" stock, which influences success probabilities throughout the development pipeline. This creates an interesting dynamic where later market entrants face lower technical risks due to accumulated knowledge, but also lower potential returns due to decreased unmet need. This dynamic was supported by stakeholder interviews that described how later development programs could build upon the learnings from earlier successful (and failed) attempts.

The model uses these feedback loops to capture how market saturation progressively changes the risk-reward calculation for drug development. Initial market entrants face high technical risks but high potential rewards, while subsequent entrants face lower technical risks but must differentiate themselves in an increasingly crowded market. This differentiation necessity is represented in the market access subsystem, where approval rates for new products become increasingly dependent on demonstrating additional benefits in terms of safety, efficacy, or cost-effectiveness compared to existing treatments.

This market dynamic creates a natural progression in drug development focus over time. The model shows how initial development efforts typically target broad efficacy for the general patient population, while later development programs are more likely to focus on specific patient subgroups or improved safety profiles. This progression is represented through changes in the Target Product Profile (TPP) parameters over time, with later entrants typically requiring more specific or stringent TPPs to justify market entry.

These interconnected feedback loops help explain the observed pattern in antiviral drug development where initial successful market entry often triggers a wave of follow-on development, but this wave eventually subsides as the market becomes increasingly saturated and remaining unmet needs become more specialized. The model can be used to simulate how different levels of initial unmet need and knowledge accumulation rates influence the timing and extent of this development wave, providing insights for both drug developers and policy makers in prioritizing development efforts.

Deviations

The submission timeline for this deliverable has experienced significant deviation from the original project plan. This delay can be attributed to two primary factors. First, there were cascading dependencies with other WP3 deliverables that needed to be completed before this work could be finalized, as they provided essential input for the model development and validation. These preceding deliverables also experienced delays, which directly impacted our timeline. Second, we encountered practical challenges in data collection and stakeholder engagement, particularly in scheduling validation sessions with consortium partners. The complexity of coordinating across multiple organizations and the busy schedules of key stakeholders made it difficult to arrange the necessary validation meetings in a timely manner. While these delays were unfortunate, they were necessary to ensure the quality and accuracy of the final model, as proper validation and stakeholder input were essential for creating a reliable representation of the antiviral development system.

The scope of this deliverable has also evolved from its original conception. Initially, the project intended to focus specifically on assessing the impact of small molecules lab activities at KU Leuven. However, as our understanding of the system developed, it became clear that a broader perspective was necessary to capture the full complexity of antiviral development. The scope expanded to encompass all WP3 labs and their interactions with WP1, WP2, WP6, and WP8, providing a more comprehensive view of the development pipeline and its downstream impact. This expansion, while necessary for system completeness, contributed to the timeline delays as it required additional data collection and validation across multiple work packages. Conversely, we narrowed the downstream analysis to focus specifically on three key subsystems: patient dynamics, investment incentives, and regulatory approval processes. This targeted approach was driven by both practical considerations regarding stakeholder availability outside the consortium and the need to manage model complexity. While the original scope included additional elements such as manufacturing and distribution, we determined that the current subsystems already captured significant complexity, and further expansion would not necessarily enhance the model's utility for decision-making purposes. The remaining work packages (WP4 and WP5) will be integrated in the next deliverable, which aims to connect all work packages into a unified model.

This report presents the foundational model structure and equations without including specific scenario results or output visualizations. While the model's conceptual framework, mathematical relationships, and system architecture have been validated and finalized through extensive stakeholder engagement, the quantitative validation process is still ongoing. The development of this comprehensive system of equations representing the entire antiviral development process - from early discovery through to patient impact - represents a significant contribution in itself. The model successfully quantifies complex interdependencies between consortium activities, regulatory processes, and market dynamics into mathematical relationships. Translating qualitative understanding from stakeholder interviews into a concrete mathematical framework required substantial effort and multiple iterations. Once the ongoing data collection and parameter validation is complete, this established model structure will enable simulation of various scenarios to support decision-making. The final results and sensitivity analyses will be published in subsequent reports after the validation process concludes.

Conclusion

This system dynamics model represents a significant contribution to understanding and optimizing antiviral drug development, particularly in the context of public-private partnerships and pandemic response. The model's comprehensive scope and interconnected structure make it valuable for multiple stakeholder groups and applications.

Patient-Centric Drug Development
A key strength of the model is its ability to trace the complete pathway from early drug discovery through to patient outcomes. By modeling the full development pipeline - from initial compound screening through clinical trials, authorization, market access, and ultimately to patient treatment - the model creates a clear mechanism for understanding how early-stage decisions impact downstream patient outcomes. This end-to-end visibility enables stakeholders to consider patient preferences and needs much earlier in the development process. The model connects early drug discovery decisions, such as TPP selection and screening cascade design, to final product characteristics that directly impact patient care. Through its detailed modeling of safety and efficacy evidence accumulation in clinical trials, the model demonstrates how these factors influence patient treatment decisions. Additionally, the model's incorporation of market access and pricing negotiations provides insight into how these elements affect patient uptake and treatment rates. This comprehensive approach allows developers to optimize early-stage decisions with clear visibility of their impact on ultimate patient outcomes.

Consortium Analyzing Tool
The model serves as both an evaluation and decision support tool for consortium structure and operations. Its detailed representation of consortium dynamics, including governance structures, partner interactions, and resource allocation, makes it particularly valuable for designing future pandemic response partnerships. The HR dynamics subsystem effectively captures how administrative overhead increases with consortium size, while simultaneously modeling the quality benefits of collaboration through impacts on assay quality and evidence generation. These competing effects can be simulated to identify effective consortium sizes for different scenarios. The model's representation of approval delays through the monthly meeting system allows for evaluation of different governance structures, enabling stakeholders to quantify the impact of streamlined versus complex decision-making processes. Through its budget allocation subsystem, the model supports improved resource distribution, including the evaluation of reserve fund impacts and trade-offs between investing in priority versus backup series.

Investment Decision Support
The model's sophisticated handling of uncertainty and risk makes it particularly valuable for investment decision-making. Through its incorporation of random functions modeling unknown effective compound rates, variable evidence generation rates, and pandemic pressure dynamics, the model creates a realistic framework for evaluating investment decisions under uncertainty. The interconnected risk factors throughout the development pipeline allow stakeholders to simulate different scenarios and evaluate potential returns under various conditions. This capability is particularly valuable for determining optimal investment timing relative to pandemic pressure, resource allocation across different development phases, and strategies for balancing risk mitigation through portfolio diversity versus focused investment.

Interactive Policy Tool
The model's structure supports development as an interactive interface where stakeholders can adjust parameters in real-time and observe system-wide effects of local changes and interventions. This makes it particularly valuable for policy makers and other stakeholders who need to understand complex system interactions without detailed technical knowledge. Policy makers can test different market authorization thresholds and observe their impact on patient access, evaluate various pandemic

response investment strategies, and assess the impact of streamlined approval processes on development timelines. The ability to compare different scenarios through simulation and evaluate health impact metrics under various conditions makes the model an invaluable tool for informed decision-making.

Future Applications

The model's flexibility and comprehensive scope make it adaptable for future challenges. It can be updated with new data as it becomes available, modified to reflect new development pathways or technologies, and expanded to include additional stakeholder perspectives. Its application extends beyond its current focus and could be valuable for other types of drug development consortia, R&D processes, multi-stakeholder projects, and public-private partnerships across various sectors. The model structure for capturing collaborative dynamics, risk management, and investment decisions under uncertainty makes it particularly valuable in contexts where organizations must balance innovation potential against operational efficiency. By providing a quantitative framework for understanding complex interactions in collaborative development, this model represents a valuable tool for improving both current operations and future strategic planning. The model's ability to simulate various scenarios and evaluate different structural arrangements makes it an essential resource for optimizing future collaborative efforts in any development context where multiple stakeholders must coordinate under uncertainty.

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