#### **MATH+ News**

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# MATH+ Professor Max von Kleist (FU Berlin) in the Media on Innovative HIV Therapy and Al-Supported Pandemic Modeling



<u>Max von Kleist</u>, Professor of "<u>Mathematics for Data Sciences</u>" at Freie Universität Berlin, researcher at the Robert Koch Institute, and <u>MATH+Professor</u>, has been commenting in the media on two highly topical subjects: the groundbreaking new HIV drug Lenacapavir and the use of artificial intelligence (AI) in combating pandemics.

Max von Kleist combines AI and mathematical modeling with practical research to develop therapeutic measures for global health problems using interdisciplinary approaches. As part of MATH+, the mathematical

foundations for this research are supported in the <u>MATH+ Emerging Field "Decision Support in the Public Sector" (EF6)</u>.

## LENACAPAVIR: SEMI-ANNUAL INJECTIONS SIMPLIFY HIV PREVENTION

In *DER SPIEGEL* and other outlets such as *ZEIT ONLINE*, *Süddeutsche Zeitung*, and *Berliner Tagesspiegel*, von Kleist commented on the results of the Phase III study *Purpose 2*, in which the new drug **Lenacapavir** was used for **HIV pre-exposure <u>prophylaxis</u>** (**PrEP**) to prevent HIV infection. Forty years after the discovery of the HIV virus, there is still no effective vaccine, nor can an infection be cured. However, the daily intake of the drug *Truvada* as prophylaxis can effectively prevent infection. In contrast, the new drug Lenacapavir required only two injections per year in the *Purpose 1 and 2* studies to achieve an almost complete protective effect. However, the degree of protection in clinical studies can only be determined with limited precision, which is a core topic of research for Max von Kleist's team.

"The efficiency of Lenacapavir is comparable to Truvada," explained Max von Kleist. "Both drugs offer outstanding, nearly complete protection. However, other factors, which are more related to social sciences, could play a role: For instance, people might find it easier to conceal the injection from their surroundings, which could prevent HIV-related stigma, particularly among women."

But von Kleist also warned: "One problem is the development of resistance. After stopping Lenacapavir, the drug remains in the body for up to a year and, at insufficient concentrations, could promote the development of resistant viruses." A follow-up treatment with Truvada might therefore be necessary to minimize this risk. "The decision of who should receive Lenacapavir under which circumstances must be carefully considered," von Kleist said.

In addition to these medical challenges, the cost issue is also critical. With a price of \$42,000 per year, Lenacapavir is unaffordable for poorer countries. Yet, it is in these regions where the drug is most urgently needed.

## On the Difference Between "Prophylaxis" and "Vaccine":

• <u>Prophylaxis:</u> A drug directly inhibits the reproduction of the virus or pathogen. Protection is immediate but disappears once the drug is metabolized. Prophylaxis is administered as a tablet or injected into fatty tissue (e.g., malaria prophylaxis).

• <u>Vaccine</u>: An antigen is administered to activate the immune system. Protection arises through a long-term immune response that develops over weeks and persists even after the antigen is metabolized. Vaccines are usually injected intramuscularly.

## AI AND MODELING SUPPORT PANDEMIC CONTROL

Max von Kleist spoke on the <u>Deutschlandfunk podcast Understanding AI</u> (KI verstehen) about the role of AI in the COVID-19 pandemic and potential future pandemics: "There were developments that were quickly implemented and provided very informed input because it was a time when one had to act very quickly based on accumulating data." AI supported efforts during the COVID-19 pandemic by analyzing health data, enhancing diagnostic imaging, and decoding the coronavirus genome, which aided drug development.

As an example of his research, von Kleist mentioned the <u>MODUS-COVID</u> project, developed at TU Berlin. The project collected health-relevant data and modeled the effects of non-pharmaceutical measures, such as school closures, on pandemic outcomes. However, von Kleist noted, "This is not a classic AI project, but rather classical modeling based on mathematical principles, where the model doesn't learn on its own but integrates available data into mechanistic models."

Von Kleist also developed his own AI algorithm to predict disease progression in COVID-19 infections. Using known data, such as the time of a positive test or symptom onset, he demonstrated how quarantine periods could be shortened through targeted testing without increasing the risk of transmission. These calculations yielded results similar to human challenge trials, where volunteers deliberately infected themselves with the virus. With this AI application, such experimental studies could be avoided in the future. However, von Kleist cautioned against overestimating the role of AI in pandemics. "It is a tool that can help but does not provide ultimate solutions," he said.

When asked whether AI is now advanced enough to save us in a new pandemic, he replied: "It is difficult for AI models to be applied to new pathogens. You don't have good training and validation datasets. Often, one simply doesn't know the ground truth," said von Kleist.

In contrast, classical modeling benefits from relatively detailed information as building blocks: "You can integrate things that are quickly learned, like infection progression. These are small building blocks that can be incorporated into a larger framework. And with that, you can make predictions more reliably," he explained. His conclusion: "Classical modeling was often more effective than AI during the COVID-19 pandemic."

## LINKS:

- Max von Kleist Research Group "Mathematics for Data Science" at Freie Universität Berlin (FU Berlin) and at Robert Koch-Institut (Project group 5)
- Max von Kleist: New MATH+ Professor of "Mathematics for Data Sciences" at FU Berlin
- Team around MATH+ Member Max von Kleist Provides New Insights Into HIV Prevention For Cisgender Women
- German media contributions featuring von Kleist on combating HIV with the drug Lenacapavir (in German):
  - DER SPIEGEL
  - ZEIT ONLINE
  - Süddeutsche Zeitung
  - TAGESSPIEGEL
  - o ZDF
- Deutschlandfunk-Podcast "KI verstehen" mit Max von Kleist (in German)