Managing the HIV/AIDS Pandemic: 2006–2055

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Summary

We begin with a thorough consideration of which nations face the most critical situations with respect to HIV / AIDS. We model an adjusted life expectancy, using a short-term logistic differential equation model, and them mathematically define criticality. By continent, we conclude that the most critical nations are: Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana.

We analyze the futures of these most critical nations with a versatile computer simulation that deals directly with people rather than homogenous populations, as a differential equations model would.

Treatment analysis includes estimation of the amount of foreign aid available through 2055 and predicts the effects of antiretroviral treatment (ART) and the possibilities of a preventive HIV / AIDS vaccine. We consider the ramifications of drug-resistant strains

We conclude with a series of recommendations for how best to allocate resources. We recommend intensive spending in the short term on research and development of a vaccine, followed by a global coverage of ART with heavy emphasis on maintaining adherence.

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Defining Criticality

Approach

What makes a country "critical"? The obvious answer is countries with the greatest number of cases, or the greatest proportion of cases; but this is not a complete analysis. A critical situation implies that progress can be made towards a solution. At this point, nothing beyond antiretroviral therapy can be done for an HIV/AIDS patient. Countries with high rates of treatment can do little more for their infected population, so such countries should not be deemed most critical. The term critical also implies that action is urgent, that HIV/AIDS will be very detrimental in the short term. We believe that the best way to measure the effect of HIV/AIDS on a population is to determine the *cumulative number of years of life lost* due to infection.

Assumptions and Terms

- ART patients have 100% adherence—a patient either receives ART treatment or not, there is no middle ground.
- No further intervention occurs within the next five years.
- ART percentages remain constant.
- No other major causes of death affect the population. Since we are predicting over a relatively short interval of time, it is unlikely that major events such as natural disasters, wars, or other pandemics will significantly affect the population.
- People-year: A unit equivalent to one person times one year. The number of people-years of a population equals the sum of all the lifetimes of people in the population.
- To measure the immediate effects of HIV/AIDS on a population receiving no further intervention, we define criticality over the next five years (2006–2010):
  - **Absolute Criticality**: The total number of people-years lost by a *population* over the next five years due to HIV/AIDS.
  - **Relative Criticality**: The average number of people-years lost by a *person* over the next five years, in other words, the change in life expectancy over the next five years.

Development

We derive a mathematical expression for criticality in terms of various parameters. Relative criticality ζ is given by

$$\zeta(\alpha, \beta, \gamma, \delta, \epsilon) = \alpha(\gamma + \delta) + \beta\epsilon,$$

where:

α is the average loss of life expectancy due to contracting HIV and without receiving ART,

β is the average loss of life expectancy due to contracting HIV and receiving ART,

γ is the number of current untreated cases divided by current population,

δ is the number of untreated cases contracted over the next five years divided by present population, and

ϵ is the number of treated cases contracted over the next five years divided by present population.

Absolute criticality is given by

$$\zeta_{\text{abs}} = \zeta P,$$

where P is the country's population.

It may seem counterintuitive that a country should be considered "less critical" if its life expectancy is innately lower, as our model would conclude. What this really means is that spending money on HIV/AIDS there may be less relevant than spending money on other causes of death.

Model A: Adjusting Life Expectancy

Approach

To determine the effects of HIV/AIDS on a population, we determine the life expectancy as if HIV/AIDS did not exist. We then adjust for the fact that life expectancy is a function of a person's year of birth.

Assumptions

- Life expectancy does not significantly change over five years, so we can assume that people of each five-year age group are the same age.
- Life expectancy data does not exist for birth years before 1950, so we assume that any person born earlier has the life expectancy of someone born in 1950.
- No immigration or emigration occurs.

Method

Using 2005 population data, we multiply the population for each age group by the life expectancy of the corresponding birth years. to arrive at the total number of person-years for the population. Dividing this by the population gives the *age-adjusted life expectancy* Γ_0.

We then determine a life expectancy value for infected people. Worldwide, we estimate that the average age for contracting HIV is 23. We assume that a person on ART has 100% adherence and never stops treatment. In developed nations, a person contracting HIV but untreated typically lives 12 years, hence on average to age $23 + 12 = 35$. Few people treated with ARV have died; however, the program began only 10 years ago. We estimate that ART patients in developed countries will live 20 years after contraction, hence on average to age $23 + 20 = 43$. To determine the average life expectancy for a person contracting HIV / AIDS, we use the formula

$$\Gamma_{\text{HIV}} = \frac{\Gamma_0}{70}\left[35(1-T) + 43T\right],$$

where T is the percentage of people currently receiving ARV treatment. The formula yields a weighted average of the life expectancies for untreated and treated patients, and we account for the difference in life expectancy due to causes other than HIV by multiplying by the age-adjusted life expectancy divided by 70, an assumed average for the life expectancy of a developed nation.

To derive an expression for the HIV-adjusted life expectancy, we take a more intuitive approach. We have data for the total number of people-years of a population, and given the number of HIV cases P_{HIV} and the average life expectancy for HIV patients, we know the total number of HIV people-years. If these people did not have HIV, the number of people-years that they contribute to the population would increase. Therefore, adding the number of people-years that the infected population loses due to premature death to the unadjusted number of people-years for a population yields the adjusted people-years, and consequently an HIV-adjusted life expectancy for that population. The formula for HIV-adjusted life expectancy Γ_A is

$$\Gamma_A = \frac{P(\Gamma_0 + P_{\text{HIV})}\Gamma_0 - \Gamma_{\text{HIV}}}{P}.$$

Expectations and Results

If our model is appropriate, a few things should certainly occur:

- The HIV-adjusted life expectancy should always be greater than the unadjusted life expectancy.
- The difference between the HIV-adjusted life expectancy and the unadjusted life expectancy should be proportional to the percentage of the population infected with HIV.

No country shows a decrease in life-expectancy after HIV-adjustment; and by taking the difference between the HIV-adjusted life expectancy and the unadjusted life expectancy and dividing by the percentage of the population infected with HIV, we find strong evidence for proportionality.

Model B: Logistic Growth

Approach

To implement our definition of criticality, we must predict the number of HIV / AIDS cases (both treated and untreated) over the next five years. A logistic growth model is easy to work with and incorporates a maximum sustainable population.

Assumptions

- Birth and death trends remain similar over the next five years.
- The incidence of HIV / AIDS is constant within each of 12 representative regions that we feel have minimal variation in HIV / AIDS growth rates: Africa, South East / Central Asia, North / East Asia, Oceania, Brazil, South America excluding Brazil, Canada, the United States, Mexico, Latin / Central America, the Caribbean, and Europe.

Development

The logistic growth model describes a population that grows in proportion to the current size of the population, in addition to factoring in a carrying capacity—in this case, a maximum sustainable AIDS population. The general form of the differential equation is

$$\frac{dP}{dt} = \frac{rP(K-P)}{K} = rP\left(1 - \frac{P}{K}\right),$$

where

P is the total HIV / AIDS population size,

r is the maximum population growth rate, and

K is the maximum sustainable HIV / AIDS population.

As the population gets closer and closer to the maximum sustainable population, its growth rate becomes a smaller proportion of the maximum growth rate r. The general solution to the differential equation is

$$P(t) = \frac{r}{ce^{-rt} + r/k},$$

where c is a constant determined by an initial condition. We must estimate k and r, using data for cases over the past 5 to 20 years. We rearrange the differential equation to the form

$$\frac{1}{P}\frac{dP}{dt} = a + bP,$$

with $a = r$ and $b = -r/k$. We then plot successive values of

$$\left(P(t_i),\ \frac{P'(t_i)}{P(t_i)}\right)$$

and fit a least-squares line to the data, yielding an estimated slope b and a y-intercept a. We estimate $P'(t_i)$ from the slope of the secant connecting the point before and the point after the chosen point.

Results

We use the above procedure to determine a function $P(t)$ for the size of the HIV/AIDS population at a given time up to 2005. For prediction, we extrapolated by evaluating the function at 2010.

Putting It All Together

Given the HIV-adjusted life expectancy, we can determine the values of α and β for each country;

$$\alpha = \Gamma_A - 35\left(\frac{\Gamma_0}{70}\right), \qquad \beta = \Gamma_A - 43\left(\frac{\Gamma_0}{70}\right).$$

Armed with a logistic model for the infected population of each region, we extrapolate to determine the number of cases that will arise over the next five years. We then make two further assumptions.

Additional Assumptions

- The proportion of cases treated by ARV will remain unchanged over the next five year.
- The proportion of HIV/AIDS cases of each country within its respective region, H_{relative}, will remain unchanged.

$$\delta = \frac{(1-T)[P_{2010} - P_{2005}]H_{\text{relative}}}{P_{2005}}, \qquad \epsilon = \frac{T[P_{2010} - P_{2005}]H_{\text{relative}}}{P_{2005}}.$$

Finally, the number of current cases is given by our data, so

$$\gamma = \frac{(1-T)H}{P}.$$

Results

We determine absolute and relative criticality values for the 108 countries for which all the required data were available. We then use relative criticality to select the most critical countries, by continent: Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana. Fourteen of the 15 most critical nations worldwide are in Africa.

Using absolute criticality would give precedence to large nations, despite relatively mild HIV / AIDS situations.

Determining Growth Rates

Model C: Simulation of a Country with HIV/AIDS

Approach

We want a more detailed and elaborate model to forecast the long-term behavior of HIV / AIDS. We opted for a discrete computer simulation of the interactions of individuals. Such a model is much better able to cope with complicated demographic combinations, since the objects of the model are persons rather than homogeneous populations. A disadvantage is that directly simulating an entire country's population in this way is not feasible.

Assumptions

- An entire country can be modeled by simulating the course of the disease over a small representative community (population on the order of 1,000).
- Allowing the simulation to run for 10 years before introducing HIV allows for a base of existing relationships to form.
- With the exception of contraction before or during birth, all transfers of HIV occur from consensual events (drug- or sex-related) between two people.
- A person's probability of dying of natural causes is directly proportional to age.
- The effect of HIV is to multiply by some factor what would otherwise be a person's probability of dying of all other causes. This effect depends solely on whether or not a person has the virus; other factors, such as time since the virus was contracted, need not be considered.
- The sexual behavior of persons regarding number of partners, frequency of sex, etc., is essentially the same, regardless of sex and sexual orientation. The only exception is that only females can be sex workers and only males can be clients of sex workers.

- The populations of female homosexuals and bisexuals can be neglected.
- People's characteristics do not change as they grow older, except for changing stages from infant to child at age 2 and from child to adult at age 16.
- Only adults have sexual relationships or share intravenous drugs.
- A needle-sharing or sexual encounter with an infected person automatically results in transfer of the virus.

Development

Relationships

The basic tools that we use to model the spread of the disease are *relationships* and *events*. A relationship between two people can be initiated by either but to occur must be accepted by the other. An event occurs within a relationship and may result in the transfer of a virus, or multiple strains of a virus. Like a relationship, an event can be initiated by either person but must be accepted by the other. Different people have tendencies to engage in different sorts of relationships and events, and may thereby be classified into relevant demographic groups. The relationships types that we used included sexual relationships, mother-child relationships, and relationships for the social use of intravenous drugs.

Availability Pools

Formation of relationships is based on availability pools. Depending on their characteristics and on existing relationships, persons are placed into availability pools for particular sorts of relationships. A person seeking a relationship chooses an appropriate availability pool and queries it for a match. The availability pool chooses a potential match using an algorithm that attempts to preserve efficiency of data structures while providing some measure of randomness, and the chosen person is given the option of accepting or refusing the offered relationship. Either person may choose to end a relationship.

Events

A person who engages in relationships has a desired rate of events of that category. The chance of accepting an event or of requesting an event in a given cycle is based on whether or not the person has reached their satiation point for the given event.

[EDITOR'S NOTE: The authors offer further details on the mechanisms for drug-use, mother-child, and sexual relationships, as well as on abstinence, monogamy, casuality, and prostitution, which we must omit.]

Birth and Death Rates

For every adult woman who is not already pregnant, a sexual encounter with a man has a fixed probability of resulting in pregnancy. (Menopause is not taken into consideration.) Every pregnancy results in the live birth of a baby nine months after conception, unless the mother dies earlier. The probability of death by natural causes is assumed to be directly proportional to age. Additionally, children (especially infants) without mothers have a constant term added to their probability of dying. When HIV is present, the death rate as if it were not present is multiplied by a fixed constant; in a sense, the virus reduces a person's "death resistance."

Data and Parameter Values

The risk of a child contracting HIV during pregnancy and birth ranges from 15% to 30%, with the risk increased another 10% to 15% due to breastfeeding over the first two years of life [Orendi 1998]. We divide this range in half to determine the rate per year of breastfeeding contraction.

The demographic data come largely from the Central Intelligence Agency [2001].

We determine the percentage of the population using IV drugs by assuming that this value equals that of the surrounding region [United Nations Office on Drugs and Crime 2005]. To determine the acceptance, seeking, and breaking rates for drug relationships, we make reasonable assumptions based on reading about the typical social behavior of IV drug abusers. We use such an approach also in determining the maximum number of drug relationships and the rate of drug relationships per year [United Nations Office on Drugs and Crime 2005].

The HIV vulnerability parameter comes directly from the HIV-adjusted life expectancy model, and is simply an adjusted ratio of the HIV life expectancy and the unadjusted life expectancy.

We discern nearly all of the parameters for sexual relationships from Francoeur et al. [2004] and the Mackay [2000].

In connection with our assumption that a person's probability of dying is directly proportional to the person's age, we need to ascertain the constant of proportionality k based on the life expectancy. The statement about the death rate can be expressed as

$$\frac{-dP/dt}{P} = kt,$$

where P is the probability the probability of a person being alive at time t. (On another scale, P is the number of people born in the same year who remain alive after time t.) Solving, we find

$$P(t) = P_0 \exp\left(-\tfrac{1}{2}kt^2\right),$$

which—surprisingly (or not, if you are already familiar with this model for human aging, which we weren't)—turns out to be proportional to the right half of a Gaussian distribution.

To combine this equation with life expectancy, let r represent the death rate and consider that for a differential time quantity dt, the expression $-r\,dt$ represents a differential quantity of people who die at age t. Hence, the average age of death, or life expectancy, is

$$\frac{1}{P_0}\int_0^\infty rt\,dt = \int_0^\infty kt^2 \exp\left(-\tfrac{1}{2}kt^2\right)\,dt.$$

We calculate this integral numerically as a function of k. [EDITOR'S NOTE: In fact, the exact value is $\sqrt{\pi/2k}$.] Setting the result equal to the life expectancy calculated from other data for the country of interest lets us determine the relevant value for k.

Results and Discussion

After running the 50-year simulation a number of times, we noticed that there was almost always an initially explosion of HIV cases in the first few years, followed by much slower growth. This is likely the result of our assumption that every encounter results in the transmission of HIV; because of this, HIV spreads very quickly through relationships that were already in place at the beginning of the 50-year period.

Additionally, as time progressed, the HIV/AIDS population appeared to approach a steady state, or infected carrying capacity. Based on the structure of our model, the majority of the adult population ends up being infected with HIV, while only a small portion of children contract the virus; the steady-state value is merely a high percentage of the steady-state value for the adult population.

Model D: Treating the Pandemic

Approach

We determine the available funding to each of the critical countries and to the world as a whole for the years 2005–2055. Then we add additional parameters to the computer simulation model to determine the effects of increased antiretroviral therapy and preventive vaccination. Further simulation, devoting different proportions of the available funding to ARV and vaccinations, allows us to determine the best way to spend both national and worldwide HIV/AIDS funding.

Assumptions

- Economic trends remain relatively stable over time.
- Inflation in the cost of HIV treatment is comparable to that of the rest of the world economy.
- ART patients have 100% adherence.
- Vaccination, when developed, is 100% effective in preventing contraction of HIV.

Finding Aid

In 2004, $6.1 billion was provided in foreign aid for HIV/AIDS, worldwide. [Agence France-Presse 2004]. To account for the growth of the world economy and the increasing awareness with respect to HIV funding, we model the available funding A (in billions of dollars) exponentially, choosing the growth rate based on recent trends in funding:

$$A_{\text{world}}(t) = \$6.1 \times (1.05)^t.$$

We then analyze the funding available to each of the six critical countries. Of the funding for HIV/AIDS in developing/semideveloped nations, 85% comes from foreign aid and 15% from domestic spending [Martin 2003]. We assume that a government spends one-twentieth of one-percent (0.0005%) of its GDP on HIV/AIDS each year. Botswana, Tonga, Bahamas, and Guyana reasonably fit this 85/15 rule; however, Thailand and Ukraine are too developed for this assumption to apply, and we impose a 25/75 analog. From this, the equations for funding are as follows, where ρ is the growth rate of the GDP for each nation.

$$A_{\text{developing}}(t) = 0.0005\text{GDP}\left[\rho^t + (1.05)^t \frac{85}{15}\right],$$
$$A_{\text{developed}}(t) = 0.0005\text{GDP}\left[\rho^t + (1.05)^t \frac{25}{75}\right].$$

The predicted cost of supplying ART is $1,100 per person per year, and we assume that a person continues ARV treatment until death. We account for the potential inflation of costs, again using an exponential function, with growth rate of 2%. The maximum number of ARV patients that a nation can treat equals total funding divided by the current cost per person.

But what are the effects on the population of an increased number of patients treated with ARV? People strictly adhering to ARV treatment have extremely suppressed HIV virus figures [Porter 2003]. This means that is nearly impossible for a correctly treated ARV patient to transfer the virus to an uninfected person. Therefore, in our modification of the computer simulation, we prevent any person treated with ARV from transferring HIV to other people. This

change should lead to a significant decrease in the number of new HIV cases per year in comparison to the original model. In theory, if all HIV cases are treated with ARV, over time the virus should be removed from the population.

In determining when a preventive vaccine will be developed, we assume that research funding is from the worldwide aid pool and that changes in funding do not have a significant effect on when a vaccine will be found. Thus, the probability of finding a preventive vaccine should be a function of time. Multiple sources state that a vaccine will not be found within the next 10 years, so we define the probability of a vaccine being discovered by a given year as

$$S(t) = .03(t - 10), \qquad \text{for } 10 < t < 43.3,$$

where time t is measured in years after 2005. This probability function assumes that in 26.7 years, there will be a 50% chance of a vaccine being discovered.

Model E: Preventive Vaccine Distribution

Approach

To model the rate of vaccine introduction, we use a logistic growth model.

Assumptions and Terms

- The steady-state percentage of the population vaccinated will be equal to that of DTP_3 and Tetanus for infants and adults respectively, as reported by the WHO in 2002 in the datasheet accompanying the problem statement.
- The steady-state percentage value will remain constant over the next 50 years.

Development

We let V be the percentage vaccinated, λ the initial growth rate, and D the maximum percentage vaccinated. The logistic model leads to

$$V(t) = \frac{D}{C\exp(-\lambda t) + 1}.$$

We determine values for λ and C from initial conditions. We assume that in one year the vaccination rate would reach 10% of its maximum value and after 10 years would reach 95%. These conditions lead to

$$\lambda \approx 0.571, \qquad C \approx 15.9, \qquad V(t) = \frac{D}{15.9e^{-0.571t} + 1}.$$

Table 1 shows the values of D for the critical countries.

Table 1.
Maximum percentage vaccinated (D) for the critical countries.

Country	Child	Adult
Botswana	87	49
Thailand	97	90
Tonga	90	93
Ukraine	99	37
Bahamas	86	1
Guyana	91	1

Model F: Resistant Strains and Mutations

Approach

One of the most dangerous aspects of the HIV virus is its ability to mutate quickly. If a regimen of treatment does not destroy or incapacitate all of the viruses in a system, only the strong ones will remain to repopulate, over time forming a dangerous resistance that renders the drug useless.

The antiretroviral therapy associated with the HIV virus is difficult. Patients must take scores of pills, multiple times per day, for the rest of their lives; we cannot expected 100% adherence to the regimen.

Assumptions

- All people receiving ART intend to maintain 100% adherence. No patients are opposed to being treated for psychological, ethical or spiritual reasons.
- No patient is guaranteed to succeed in maintaining 100% adherence.
- A person with cumulative adherence below 90% has a 5% chance of developing a resistant strain.
- The opportunity for a resistant strain to develop occurs every time a treatment occurs in which cumulative adherence is below 90%.
- ART for a resistant strain will not be available before the year 2055. This allows us to make the simplification that only one resistant strain will exist.
- Resistant strains can be vaccinated against, but a new vaccine will have to be developed.
- The only property of a resistant strain that distinguishes it from the original HIV is the resistance to ART. The effects on the body and on life expectancy remain constant.
- The resistant strain, if it exists, takes precedence over the original strain, that is, a person will not carry both.

Development

We assume (with no data basis) that a person will adhere completely to a year of treatment 99% of the time.

By creating a new parameter within the main simulation, we can simulate the adherence behavior of every ARV patient within the model. A second parameter randomly decides whether a person with sufficiently low adherence (less than 90%) causes production of a resistant strain. We introduce a constraint on this behavior, not allowing resistant strains to occur within a person until after three years of treatment. This constraint minimizes the skewing effects that could occur if a person developed a resistant strain after missing the first treatment, which is biologically nonsensical, as the virus would have nothing to resist. The computer simulation runs as before, allowing for a resistant strain to occur. This strain would not be affected by ART or vaccination, and thus resistant-strain-infected people would behave like HIV-infected people who remain untreated.

Given that second- and third-line ARV drugs are so expensive, we assume that none of our critical countries will have access to them. We assess the probability of developing a vaccine against the resistant strain as

$$S_{\text{resistant}}(t) = .03t, \qquad 0 < t < 33.3,$$

where t is the number of years since finding the original vaccine to the non-resistant strain. We assume that the costs associated with the new vaccine are identical to those of the original vaccine.

Discussion of Models D-F

Assuming no economic disasters over the next 50 years, the world economy is well prepared to handle the HIV / AIDS situation and should be able to provide billions of dollars to the cause consistently. The question is not about availability of money but where to spend it.

ART is a powerful weapon; it almost certainly prevents transfer to uninfected people. There is, however, the danger of production of resistant strains of HIV. It is vital that the implementation of ARV programs be done with great emphasis on maintaining adherence to the program.

A preventive vaccine would provide quickly stall new cases and bring the disease down to a manageable level. We believe it probable that a vaccine will be discovered within 25 to 40 years. It is important to devote resources to its research and development.

We suggest that funds be allocated largely to ART in the next few years to bring raging epidemics in the critical nations under control, followed by a phasing in of an intense vaccine development program beginning in approximately 10 years.

Conclusion

The critical countries by continent—Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana—are a springboard for a global control effort of the pandemic.

Foreign aid should be focused on the most critical nations, not necessarily by continent, but worldwide. Treatment should begin with sweeping programs of antiretroviral therapy focused on maintaining 100% adherence. Simultaneously, research should begin on developing a preventive vaccination, which could begin distribution immediately and reach stable levels within 10 years.

Strengths and Weaknesses

Weaknesses of the model included assumptions made for simplicity that likely do not hold. For instance, in most runs of our model on any country, cases exploded rapidly to include most of the adult population within three years—a feature that does not correspond to the past behavior of HIV. This feature is likely a result of our assumption that every single sexual encounter or sharing of a dirty needle with an infected person results in disease transmission.

However, a corresponding strength of our model is that it would be relatively easy to include a parameter for probability of transmission.

Our model is particularly appropriate for simulation of evolving strains of resistant viruses, a problem that naturally lends itself to such discrete modeling.

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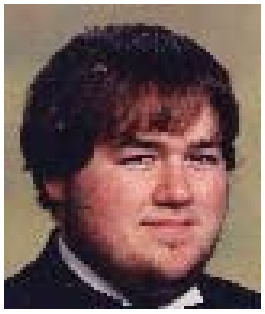

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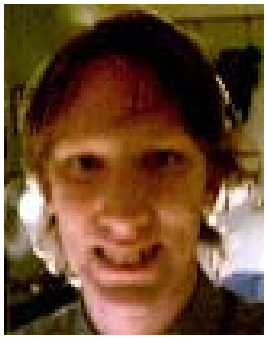

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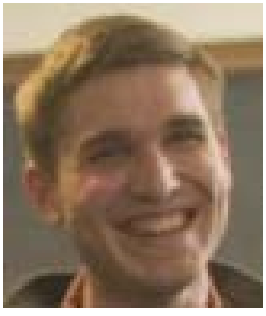

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