PROFESSOR: So in the majority of cases of indoor spreading that occur over the space of hours or even a few days, the Wells-Riley model of slow incubation where the number of infectors is held constant at the initial value, is a reasonable approximation.

For COVID-19, the incubation period is estimated to be on the order of several days.

For example, a number of 5.5 days is often quoted as an estimated mean incubation period.

On the other hand, in some cases there are spreading events that involve people interacting over much longer periods of time than that.

A famous example, which is a little bit longer than the time of incubation, is the case of the Diamond Princess cruise ship, which was quarantined in Yokohama Port, Japan in early 2020 when it was detected that there were a number of cases onboard.

The exact number wasn't known because they hadn't tested the entire population, but there were several cases.

And so they decided to quarantine the ship for 12 days.

And if you look at the number of infections versus time once they started testing and felt they had a good sense of the numbers, you can see that it rose from value, which we may estimate to be on the order of 20 possible cases initially.

And it rises, but in a very non-linear fashion.

In fact, it starts to accelerate and go steeper and steeper.

Now recall, the Wells-Riley model cannot possibly predict this behavior because if you have a fixed number infectors, then at first you have a certain rate of transmission but it always has to slow down because if there's no new infections, the same factors are running out of susceptible people to infect.

The number of susceptible is going down, and so you kind of slowly saturate until eventually you've infected everybody, when it's just one person or a fixed number of people who are basically transmitting at a constant rate of infection quanta to everybody else.

But that's not what happened.

In fact, it's a very steep rise.

It went-- just in the last few days, it jumped by several hundred people.

And in fact, if they hadn't stopped the quarantine in 12 days-- there were 4,000 people on that ship.

I think 3,711.

I'll just mention I think that was the number.

So way higher.

And you see how this is accelerating.

If they'd gone with the quarantine a couple more days, they might have had thousands of people infected.

So in fact, this is an interesting warning for quarantines, that just cooping up some people for 14 days doesn't make everybody safe.

If many of those people are susceptible and are not yet infected, they can become infected.

And many interesting things about this incident is that the people were not in direct contact, obviously.

Thousands of people were not six feet apart from each other.

They were often in different rooms, different floors of the ship.

And yet, very large numbers became infected in a short time.

So the important thing I'd like to emphasize now coming back to our SEI model is that this sort of non-linear increase can only be explained if you have some accelerated spreading due to new infected people.

And it makes sense after about five days.

And we also don't know when people got infected.

So those initially infected people may have been infected five days earlier.

So there may have been already an increase in the number infected people already at time equals zero of the quarantine.

And so we should now account also for the exposed people.

Those are people that may not be showing symptoms yet, but have been exposed enough that they can then pass it on.

And so the rate of an exposed person becoming an infectious person is alpha.

And inverse of alpha is that 5.5 days.

So that's the incubation time.

And this might be something like 5.5 days for COVID-19.

But of course it can vary.

But it's roughly in that order.

And so it makes sense to look at the Diamond Princess and consider what would be the effect of accounting for incubation.

So these are non-linear equations that don't have a simple solution to the full model.

But in the same way the Wells-Riley model is the limit of slow incubation, where basically E stays zero and basically you only have infected people.

Now, we can consider the opposite limit of fast incubation.

So let's consider the opposite limit of fast incubation.

And this would be alpha t much greater than one.

So basically, we want to make sure that the t is much bigger than the incubation time.

And as I said, the incubation time doesn't necessarily start at time zero.

The infected people in this case may have already been infected five days earlier.

In fact, the cruise ship had been going for actually weeks before that.

So no one knows exactly when the infection began.

So it may be even likely that that was happening.

So let's consider the fast incubation limit.

So what this then tells us is that now the exposed portion is roughly zero.

So if alpha is very quick, then you pretty much quickly go through the exposed, and you end up immediately being infected.

And so this is actually a much simpler model where the number of susceptibles is just n minus I.

So there's no exposed compartment anymore.

So the Wells-Riley model in some sense is the SE model, where there are only exposed people and susceptible, but the number infected doesn't change.

This is really the SI model, where we don't worry about the exposed compartment, OK?

So the equation we want to solve then, if we realize that S is n minus I is that dS dt is minus beta of t SI.

So that's the same equation I wrote down earlier.

But now let's substitute.

Let's derive an equation for the number of infected.

So that will be from here, dI dt will be beta of t times I.

And then S is n minus I. Because again, if we go straight through the exposed fraction, then basically this rate of losing susceptibles is equal to the rate of creating new infected people.

Again, because n is fixed.

The number of people is fixed.

So dS dt is minus the dI dt.

So this is the equation now that we can solve for this limit of the model.

And fortunately, this is a simple equation to solve.

It's a first order separable differential equation.

So we can write this as dI over I times n minus I is equal to beta of t dt.

On this side, I can write this as-- I can factor out a one over n, and write this as one over I plus one over n minus I. So when I combine these two, I get In minus nine in the denominator.

And the numerator, I get n minus I plus I. So just get n.

But then it divides by that n, so I do come back to what I started with.

And this times dI.

And so now I can integrate both sides this equation.

Take into account the initial condition is that at t equals zero, the number of infectors is I0.

So basically, I can integrate by going from zero to time, t.

And on this side, in terms of the infectors, I'm going from I0 to the current number of infectors, I.

OK, so now we're ready to integrate this equation.

So let's multiply the n to the other side and do the integrals.

So basically, the integral of one over I is log I.

So we have log I minus log of n minus I.

And that's because there's a minus I there, so that leads to a minus sign out front.

On the other side, if I multiply through by n, I have n integral from zero to t of beta of t dt plus a constant of integration.

The boundary condition that I need is that I of zero is I0.

So a t equals zero, this term vanishes, and this expression must be evaluated with I equal to I0.

So therefore, there must be on this side of the equation, some constants log of I0 minus log of n minus I0.

So now we satisfy the boundary condition or initial condition of t equals zero.

Now, I can also write this in terms of the quanta emission rate for the initial infectors, which we defined earlier.

So for the Wells-Riley model, we talked about writing q of t is the number of quanta emitted by the initial infector.

So if we just define it as I zero times the integral over time of beta of t dt, this is the sort of infection quanta emitted by the I0 initial infectors.

So if we take that here, we can express the solution a somewhat different way.

If I take an exponential on both sides, the difference of two logs is the log of the ratio.

And when I exponentiate, I get rid of the log.

So this side turns into I over n minus I. And the other side, we have from the similar expression, I0 over n minus I0.

But times, now, the exponential of-- well, if we want to express it in terms of q0, it would be n.

And then this d beta dt has a one over I0 q of t.

So this is the solution in this case.

Now, if we look at early times-- and so then that would be less than incubation time.

So if basically our alpha t is much less than one-- so not much incubation is occurred.

And basically during that time I is approximately still equal to I0.

So that would be kind of in the early, early stages here of this dynamics-- then we could write that I of t is, well, from this we could write it as n minus I0.

And then I0 times the time interval of beta, or n minus I0 times q, or it's the number of susceptibles times q of t.

So this is a result that can come directly from analyzing this expression.

We can also see it here, that if I is not changing, then we have I, n minus I. And we can also see this expression here where we just integrate both sides in time to get to this equation here.

So it's basically the same as the Wells-Riley in an early time.

And that's an interesting observation, which is that there is a universal sort of small transmission limit in both limits of this model.

And what that is, if we take this-- at least for the SEI model, if we write how many exposed plus infected relative to the initial number of infectors, OK?

So that is telling us how many transmissions there are, either to make someone exposed or to make them infectious from the initial number of infectors.

That at early times, we get this same result that we had before because we got the same thing for the Wells-Riley model for E, here it's for I. And we find that this is this what we call Rn, the indoor transmission number.

Which is the initial number of susceptibles times the number of quanta transferred.

And in the case where if S0 were equal to n minus one, and I0 were equal to one, this would be n minus one integral over t of beta dt.

That would be that case that we talked about before for the indoor transmission number.

But more generally, it would look like this.

So that is at early times, before many transmissions have happened.

It really doesn't matter what's the details of the model in terms of the non-linear response.

So even if after a longer amount of time more and more people get infected, the initial moments are always universal and are really just governed by this transmission rate beta and the number of susceptible people and number of infectious people initially in the room.

So it's kind of independent of all these details here.

And so then to kind of summarize that picture, we could plot versus time here what happens in terms of the-- so we have a rate of transmission where if I look at the total number of exposed plus infected people, OK.

And then here's the total number of people in the room, n.

So in the Wells-Riley model, everyone's exposed, but nobody becomes infectious.

And we know that we get this kind of exponential relaxation as we eventually run out of susceptible people.

And the timescale for that is beta inverse, OK.

And that gives you the transmission time for just a fixed number of infectors to slowly infect everybody else.

But in the case like we described here where we have some non-linear acceleration, that has to start out the same.

That's what I'm trying to say here, is the initial transmission rate doesn't matter if there is an incubation rate until you reach the incubation time.

So there's kind of an alpha inverse here, which is the incubation time.

This one here is the transmission time.

And at this time scale, you start to see an exponential increase until it saturates basically once all the transmission has occurred because now there's more and more infectious people.

And so this is the fast incubation and slow incubation.

And this one is the Wells-Riley model, which is widely used.

But if you're fitting spreading data where there may actually be some incubation going on, and also potentially removal-- we could add another equation for the removal of people.

We need to be careful on how we fit data in order to extract information about the transmission rate, which is what we're interested in what we're trying to interpret the data.

So maybe an important conclusion from this is that infection quanta, this notion-- or the infection quantum, I guess you can say, one of them.

Which is a quantity that was introduced by Wells, really based on this Wells-Riley model, is basically-- think of this exponential relaxation, and saying when let's say 63% of people become infected, that's what you say is one infection quantum has been transmitted to each of those people.

Then really, it's better defined-- I'll just write here it's defined by the transmission rate and not by the number of people that actually get infected.

So if you look at some data like the Diamond Princess or other data that we're going to look at later, you are seeing spreading happening and there could be lots of contributions to the number of people that actually get sick.

For example, there could be incubation going on.

So what's sometimes called the secondary attack rate is E plus I divided by S0.

So the secondary attack rate is sort of the fraction of people that are susceptible that got infected.

And the Wells-Riley would say, when that 63% then you've transmitted a quantum to each of those people.

Whereas, as we see in the case of the fast incubation model, that's not how you would interpret that data.

But on the other hand, beta is well-defined.

It's just each person is transferring quanta at a certain rate and has the potential to infect other people.

Now, I don't want to overstate the relevance of this model for a particular case like the Diamond Princess cruise ship.

We'll come back to this later.

But just simply to illustrate that it has this kind of non-linear feature which is suggestive of incubation occurring and an increase in the number of infected people.

And just to point out that this sort of simple modeling leads us to kind of a universal expression for the initial transmission from the initial in factors for each of them to transfer to sort of one other, which is this indoor reproductive number.

And that's really what's valid at the early times here.

And that's where we have kind of a universal behavior.

And that's useful in formulating safety guidelines, which we will do next.