Podcast Transcript

C: Chloe from WashingtonJ: Jess from Sydney_AustraliaL: Lukian from Sydney_AustraliaO: Owen from WashingtonS: Sylvie from Sydney_Australia

Tone indicators used: /s: sarcastic /j: joking All sentences should be taken non-sarcastically and non-jokingly unless otherwise stated by tone indicators.

S: Welcome everyone. This podcast is part of a collaboration between the Washington and Sydney iGEM teams. We're doing this collaboration because we realise that both of our projects have a strong focus on at-home diagnostic testing technology. So, the Washington team is working on a genetic test for cutaneous melanoma and the Sydney team is working on generating novel nanobodies that could be applied in rapid-flow assays. So we're planning on discussing some of the impacts of diagnostic technologies in the context of the differences in the healthcare systems in both countries. So we thought that the applications of our tests might look really different in our two different countries: the US and Australia. We'll start with some introductions. I'll let the Washington team introduce themselves.

O: Hi, I'm Owen.

C: Hi, I'm Chloe.

S: And the Sydney team...

L: Hi I'm Lukian.

J: And hi everyone, I'm Jess.

S: And I'm Sylvie. Despite my American accent, I'm on the Sydney team. I'm a bit of a transplant. I'm acting as a sort of moderator because I have some experience growing up in the US and experience living in Australia as well.

Before we get into it I would just like to do an acknowledgement of country.

We would like to acknowledge the traditional custodians of the lands where we are living and working on today, the Gadigal people of the Eora Nation here in Sydney and the Duwamish, Puyallup, Suquamish, Tulalip and Muckleshoot nations in Washington and their elders past, present and emerging.

So, we'll start off by just giving a comparison of the healthcare systems in both countries. Both of our projects have applications in diagnostic testing. One of the biggest differences that most people know about when it comes to healthcare in Australia and the US is the cost to the patient. Owen, do you want to give us an idea of how healthcare costs look in the US?

O: Right, so we've got some fun numbers here /s. Australia is actually about average on healthcare spending. Austrliains spend about \$5600 per capita. Americans spend more than double that, we spend about \$12,000 on healthcare. A lot of that goes into admin costs, so it's not going toward care. The US actually tends to have slightly worse health outcomes than other developed countries like Australia, so we're getting less bang for our buck. Part of that is...

J: Why do you think that is, Owen?

O: So part of that is, unlike almost every other developed country in the world, the United States uses a system that relies almost entirely on private health insurance, most of that provided by people's employers. We do have a little bit of state provided insurance. We've got Medicare which covers folks over 65, and then we've got Medicaid which provides some support for people with low incomes, but that's also managed by each individual state. So it varies widely across the country. So all this variation makes the cost of actually providing healthcare really high. Not even the cost of actual treatments and doctors but just like managing all the paperwork. We have become a country of paperwork in our healthcare and that's not super great for the outcomes.

J: And with things like Medicare and Medicaid, do they cover... can you expect to walk into every clinic and know that they're going to be covered by that sort of thing? Or can you expect every clinic to be covered by the same insurance? How does that really work?

O: So that whole network of systems means that a lot of providers don't actually take, or won't take your insurance, or they'll take your insurance but then they won't take other things. So the system is very patchwork. Some places will take medicare but then won't take things like Medicaid. Since our project is focused on melanoma, it is good to know that Medicaid is actually taken only by about 16% of dermatology clinics in the US. So a lot of that specialised care like dermatology you can't get coverage for. And both the coverages provided by the federal government don't cover stuff that's called cosmetic surgery or anything. It's like if you don't need that, they're not going to pay for it so there's a limited range where the system's even going to help you out, even if you have insurance that should cover care.

J: And if I'm right you said Medicaid was the one for elderly, or was it Medicare?

O: Okay yeah, so this one is very fun to keep track of /s. Medicare is for retired people, it's limited to over 65, or folks with disabilities. Medicaid is just for people with low incomes.

S: Which is slightly confusing because in Australia, our national government health insurance is also called Medicare, but that's for everyone. I guess Medicare is just too good a word to let one country have.

J: Lukian do you want to talk about how Medicare works in Australia? It's a bit different.

L: Yeah, so we have Medicare which is a pretty good system I would say. If you're an Australian citizen, New Zealand citizen or a permanent Australian resident, you're eligible for Medicare. That means that most basic medical services are covered. So we have what's called bulk billing, so if you're bulk billed by your doctor, and that can be sort of a GP, specialist or anything medical, means that it's entirely covered by Medicare, and it means you don't have to pay for it. So generally when you arrange a doctor's visit, you can ask them if they will bulk bill or not, which gives people the option to shop around and find places that will bulk bill. And obviously that makes things pretty... it means that people aren't scared to go to the doctor because they're worried about the bill they're going to get, especially with GPs. I'm not sure what it's like in America, but in Australia, GP is just your general practitioner, and if there's anything slightly wrong with you, if you're feeling one way, you just go. You just go straight to the GP.

S: Yeah, I mean from my experience living in the US, I know that there's a really high number of people that avoid going to kind of preventative care visits, or visiting a doctor for minor things just because of the cost. So I think there's a bit of a different culture at least here in Sydney, of being a bit more proactive in preventative care.

L: If you ever go to the hospital, the emergency department is free.

J: Yes, ambulances are free.

L: So if you've broken your leg, if you've stepped on a nail, you're not desperately trying to fix it at home. At least once a year I hurt myself enough that I go to the ED, I wait for a couple hours, it gets dealt with and then that's it. There's no cost, it's just done.

J: Yeah.

C: I wanted to ask, since Owen mentioned a lot of our cosmetic surgeon things aren't covered, are there any grey areas to Medicare in Australia? Or it is like most things are genuinely covered by your healthcare policy?

J: So similarly, things that are deemed cosmetic won't be covered. One interesting controversial thing is dentistry. The dentists aren't covered, so I think they've considered the rest of your body more important than your teeth. Not really sure why that is. It is good, you can get referrals for a lot of things, like for specialists that do get rebates. But yeah, melanoma or skin cancer dermatologist side referrals, I think that might be a difference in the

way that the two countries view skin cancer, because I think that is definitely not going to come under cosmetic surgery in any case in Australia. It's taken very seriously.

S: The Washington team's project is focused on developing some at-home genetic testing for melanoma. So I think it would be interesting to compare the process of investigating maybe a concerning mole, which you are concerned might be cancerous. What would be the process of getting that looked at in Australia?

L: The Cancer Council is a big organisation in Australia. Given how much skin cancer we get, and how big of a problem it is, we're constantly... the big thing is prevention, it's a huge deal in that we're constantly bombarded with "wear sunblock, wear a hat, don't go outside in the middle of the day." It's hard to be ignorant about skin cancer, so I think a lot of the onus to test is actually put on yourself. So if you go to the Skin Cancer Council guide, they basically just give you a big list of instructions on how you test yourself for skin cancer, these are the things you want to look for. Because skin cancer is so common that if you went to the doctor every time you saw a mole, doctors would not have time to see patients... ever. A lot of it is that you have to be pretty sure that you have it, and then you'll go book into see a GP, they will go "no you've got nothing to worry about," or they will look at it and they say "yeah, that looks like it's probably skin cancer," and they'll refer you on to a dermatologist.

J: Yeah, especially the part about the onus being on the individual. I think there's a lot of focus put into public health measures education-wise and empowering individuals themselves to be able to look after themselves in that regard because everyone is at such high risk. Which I think from what it sounds like, your project fits into that picture right? That's sort of the kind of thing you want to do with your testing in the States.

S: Yeah, were there any parts of that process that would differ in the US?

C: I would say that generally it's about the same type of process. I mean here we do go to a general doctor if you're concerned. And then they obviously will refer you to someone like a dermatologist or someone that could further check it out because they're not specialised. But I think that most of it is not as... screening for melanoma at least in the US from my experience and what I've heard is that it's not as prevalent, it's not as pushed in order to go check the moles or to really take care of yourself in that aspect to make sure you don't have any type of skin cancer. I think at least with our project, trying to push that emphasis on getting tested and having more people just kind of self aware of what the possibilities could be if they don't get certain moles checked out. Owen if you want to add on to that...

O: I think just what you were saying about the individual responsibility component in Australia is interesting because America likes to be like "we're the country of individual responsibility" and that's how it goes, and that's how it's going to keep going. I think that in Australia, there's at least this responsibility put on the person like "you've got to go check for melanoma," but there's also a hand to guide you to be like these are the signs for melanoma, here what you need to do. And that there's a path forward, it's just on the person to follow the

instructions and be generally careful. Whereas, in the US, there's pretty much no public awareness about melanoma, and then that's paired with a healthcare system that's very different place-by-place. And then the insurance nonsense that we were talking about before is a fun contributor because you're going to need to get a referral to get any coverage at all, and then sometimes you can't, even if you get a referral, get coverage if they don't take whatever your coverage is especially if that's gonna be Medicaid or something like that. You might just be out of luck. That whole process means that people have to invest a lot more time in getting diagnosed for melanoma, and also a lot more money just because healthcare costs more here. So together that really creates a disincentive for people to actually be like "I've got a mole, let's do something about it" just because doing something about it is going to take you 12 hours overall to get it done, that's a real barrier to actually getting any treatment.

L: I think a big thing in Australia is even if it did cost so much, even if it was a 12 hour commitment, people are aware of how dangerous it is, and are scared enough of skin cancer that they will like drop everything to get tested. Because I know that two thirds of Australians get skin cancer over their lifetimes, and I know that that sort of differs a lot. So I surf, and surfers are six times more likely to get skin cancer. I believe 90% of surfers get skin cancer over their life. So if you're someone who goes outside a lot and if you have that risk, if you see it, you're going to deal with it immediately, because basically every Australian knows someone who's had melanoma, like been seriously ill from melanoma.

J: Maybe the Washington team needs to hit up the surfing community, reach out to them /j.

O: Fortunately in Washington, if you want to go surfing, you have to wear a full-body wetsuit so you're not going to get any sun at all.

J: Maybe down the coast in California.

C: Oh yeah, in California I think you do need a wetsuit too.

L: Well even with a wetsuit I know that a lot of the surfers I know, you look at their arms and legs and everything and they're fine, and then you look at their hands and face, and they've all had twenty, thirty moles dug out. And you just see scarring all over people's faces and hands because those are the parts that aren't covered.

S: One really interesting thing with the Australian skin cancer prevention thing that I noticed, because I did about a year of primary school in Australia. I grew up mostly in the US but when I went to primary school, I think it was year five, whenever you went outside you had to wear a hat.

J: Yeah, no hat, no play.

S: You had to wear a really wide-brimmed hat, and that was just not a thing in the US at all. I guess you could wear a hat but it wasn't this overarching, very strict rule that you had to wear a hat at all times when you were outside. I think that is a very big difference in the attitudes.

J: Yeah, teachers walk around outside and you get sent inside if you don't have your hat on. Because you can get detention for repeatedly not wearing your hat during lunchtime.

S: There are all these little primary school kids wearing these giant wide-brim hats that you would just never see in the US. In a country where this preventative attitude really isn't present, who do you think would benefit most from this at-home skin cancer testing? Who is your target demographic?

O: I think the short answer is pretty much everyone. It's not that the people who need it is everyone. Definitely well-off folks have a lot more treatment for skin cancer and mortality is a lot lower. The really unfortunate part of our system is that if you're uninsured, you are two times more likely to be diagnosed with melanoma late, after it has progressed to the point where the mortality rate is a lot higher. The hope would be that a rapid test that someone can take would really help folks where it's hard to gauge where there is that risk. Is it worth spending all this time and money or not? So that really the hope would be that for folks that are uninsured or folks that find it really hard to get to a dermatologist, rural parts of the country in particular, it might be helpful to have a rapid test. Having access to dermatology is really important and so if you can motivate people to go and get access through a test, that looked at counties in the US. And they found that if you compared counties that had one dermatologist versus no dermatologists, in adding one dermatologist reduced mortality from melanoma by about 35%, which is a pretty big reduction.

J: That's a lot.

O: Just one dermatology clinic. So having that access really can change outcomes.

J: Yeah that point you made about the risk calculation, that's something that is quite mind blowing from the Australian perspective, that you have to sit there and actually assess how bad it is to see if you actually want to go and spend the exorbitant amount of money I guess. And what you said about the rural side of things, I think that is where Australia is probably like... our hole in our safety net. Because, I looked into this a little bit and 92% of dermatologists in Australia work in metropolitan areas and people in the more rural and remote areas have higher rates of skin cancer. But not only that, they're also more likely to be farmers and outdoor workers, who are exposed to more UV radiation than those living in the city. So I think definitely if we were to talk about your test being applied in the Australian context, I think if your test could be something that could be mailed out to people in that sort of remote area where you would have to travel really far to go see a dermatologist, that would also be really helpful even in the Australian context where awareness is already so high. S: Yeah, I think as well, the US does have rural areas, but Australia has huge parts of the country that are just completely inaccessible so the few people, the, what, 5% of the population that's scattered across, or less than 5% of the population that scattered across the middle bit is so spread out, so much more than you would see in the US. Australia has more of a problem getting that preventative care, specialist care, to people in really remote areas.

J: Even in those areas you were talking about, like the difference one dermatology clinic makes, you really wouldn't be able to expect a dermatology clinic in every single one of those towns. So something like your test, which could be mailed out without a person having to go along with it, I think a massive roll-out of that would be really really helpful

S: So the Sydney team, our potential application for our project is a method for easily developing new rapid antigen tests, so our product is more of a method than it is an actual product. But the potential application could be making multiplex rapid antigen tests that could tell you which strain of COVID you have, or just developing new rapid antigen tests for new diseases quite quickly. But how do you think... Do you think that would be applied in a similar context as this melanoma test?

O: Can I jump in with one quick question?

S: Yes.

O: For people like me who are maybe not the brightest /j, what does the word multiplex mean? And what is the benefit?

S: Sorry, yes, that is probably a bit of a jargon word. A multiplex assay, a multiplex rapid antigen test, would just be instead of one test line, like normally on a rapid antigen test for COVID, as we've all probably seen and taken, there's one control line and there's one test line. So instead of one test line that just tells you yes or no, you have COVID, there could be multiple test lines that could identify the particular strain of COVID that you have. Or any other disease, so it can test for multiple antigens in the same test.

J: So that sort of multiplex test is currently often clinically applied to differentiate between different other sorts of infectious diseases. So you've got multiplex PCRs which can differentiate between different strains of fungal diseases, for example cryptococcus. It would really be taking that sort of application and bringing it to something that, I guess we are positing, could be something that an individual could take home and do themselves.

S: How do you think... Jess, do you want to give your thoughts on how a more diverse range of rapid antigen tests could impact rural or low-income populations?

J: I think, not even the multiplexing, but just the ability to generate that sort of selfdiagnostic, or not quite diagnostic but take-home testing, quickly, which is the sort of method that we're generating, quickly and at a low cost, I think really does have a lot of the same principles in terms of access for those living in remote areas. Also for, in the Australian context, indigenous communities. There's been... during the COVID-19 pandemic, there was a decentralised, point of care testing model introduced in indigenous communities for that COVID-19 response. Just to explain this a little bit, the point of care is rather than having to go to a clinic and get your test sent off somewhere elsewhere, or go to someone and get referred to another specialist, the point of care model is at the point of care with the individual that you are seeing. They are doing the test, and you are getting the test back. And that testing model saw huge success. I think that take-home tests is almost a variant on that sort of point of care model where you've got the same sort of advantages of being able to reach more remote areas that are perhaps more isolated. Obviously though, that being said, there are some caveats, especially with the context of COVID-19 testing, I know Australia had some trouble sourcing our tests. Did you guys... what was it like over in Washington for testing and approval?

O: We've actually got a fun little local story about the testing and approval process in Washington state /s. Our team, Washington iGEM, is based at the University of Washington, and there was a professor there named Helen Chu who when the COVD test was... not the COVID test, the COVID pandemic was really starting to get out of control, let's see here... She was running this thing, it was called the, now let me make sure I get this right, it was called the Seattle Flu Study, and they were collecting all these swabs to test people for flu, but then suddenly there was this bigger problem than the flu. So they went to the CDC and were like "hey, we've got this test for the COVD antigen, we know it hasn't been approved yet, but we want to take these samples and test them." And basically their answer was "absolutely not, you can't do that, don't tell us valuable information about epidemiology and the spread of this virus we know nothing about." They said "you've got to follow the rules." SI they went through a couple rounds, but initially the Seattle Flu Study was like "we have to test these samples." So they started testing them with this antigen test for COVID. They found immediately that there's these folks that have COVID and they're going to school, they're going to work, they're going to worship. This is a potential hazard to people's health. So they went and they called the Washington Department of Health and said "hey, we have these people, you need to tell them that they could potentially kill other people." And the CDC response was "absolutely knock that off right now, you can't do that, we've got rules." And part of it was because they weren't certified as a clinical laboratory. Part of it was that they had people sign a waiver when they were collecting the sample originally. But all this paperwork added up so that there was this massive delay in getting testing. Unfortunately there was a carve-out in the rules, because folks saw this and they were like "we want to make sure that in a pandemic like COVID, that we're ready." And there was this thing called the emergency use authorization, and the use authorization was set up so that you could get your test approved quickly. But unfortunately, the one test that they did approve was the CDC's own test, which they passed out, and then it turned out it didn't work. So there was this massive delay, there were false test results, the correct test results weren't allowed to be used, and it really was quite a mess.

J: Wow, that sounds like a bureaucratic nightmare. Oh dear.

O: That was about all of our reactions.

S: Speaking of bureaucratic nightmare, obviously from that story, and also from my knowledge of testing approval, regulations of at-home testing can be a little tricky. Especially because at-home testing, especially the rapid antigen test approach, and this genetic test for melanoma, has lower accuracy, gives higher rates of false positive or negative results than the standard pathology testing. How do you think... If your test has lower accuracy, how do you think it fits into the wider healthcare system? Do you think that they still have a place despite their lower accuracy?

O: I can't speak to your guys' project but at least I can say for ours we ran into the same problem. We are worried about the potential for false positives, and so the solution that we came around to was to pair that with artificial intelligence that would use images of the melanoma from a dermatoscope quality, which is the little thing that dermatologist use to look your skin cancer, through your phone through a special lens. So our proposed solution would pair that with another thing and then the goal would also be instead of giving and "you got it or you don't got it" would be to pair that with something that's a little bit more qualitative, an assessment of risk. And that sounds like something that your guys's... your multiplexing test would be good at that. I don't know if that's true though. Does that sound right to y'all?

S: The issues that exist, especially with the different rapid antigen tests, will still exist with a multiplex rapid antigen test. Probably more so, because there are more variables to go wrong. But, I mean, it will definitely have lower accuracy than something like a PCR test just because PCR is so accurate and can act on such a small sample, as we've discovered through the course of our project. You can put one cell into a PCR tube and be able to amplify genes inside that cell. So I don't think any kind of antigen test will ever be as accurate as that but rapid antigen testing still really does have a place, especially in the pandemic. But it could hold a similar place for other diseases where getting a pretty good idea of whether or not you have this infection is still really useful even if it's not 100% accurate.

L: I think the thing with the take-home tests is people will actually do them. It's so much better than nothing, because a lot of the time, even in Australia where we have Medicare and things are free, people are just lazy and they're in denial, and they don't want to go and get tested for things when they're sick.

J: So true.

L: Even me personally, I can remember times when I probably should've gone to a doctor and I went "nah, it's fine" just because there's so much you have to sit through, and it's stressful, and it's better to just pretend it's not there. But with a rapid test that you already have at home you just don't have an excuse. But it takes away that little barrier. Even if there's a high rate of false positives or negatives, for the people who get a correct results, or even a false positive, it'll sort of inspire you to go and make the next step because it brings it from something that's in your head to something that's "oh, okay this could actually be quite serious."

J: Yeah, and just to add on to that, like you said it's better than nothing, it's better than not going. In indigenous communities in Australia which is.. They're communities that are lagging behind in terms of health and in terms of life expectancy. A huge barrier to access is a cultural awareness of the actual services that are provided. So a lot of times the services that are provided may not align with cultural values or they may be provided with a doctor that has no understanding of the cultural background. So take-home testing, there is a downside to having such medical information be put into your hands, and for you to be carrying that out because it increases the margin of error. But at the same time, if you're looking at a community that is unlikely to be going to the doctor as frequently, giving them a test that they can perform themselves where they feel like they have control, and the outcome is in their hands without needing to interact with someone that might be judgemental or might not have the right sort of awareness of situations, would be really beneficial.

S: So we've talked a lot about the positives of our projects. Obviously we all like to think that we're doing something that is beneficial, but certainly there are limitations. We've talked about the lower accuracy than the standard pathology screening, but what do you think are some other limitations of this style of at-home testing?

O: I would say that one of the big things, at least for our test, is that there's still a not insignificant, at least there's still potentially a not insignificant, cost barrier for ours. Your project, in making them both cheaper and quicker, helps address that for sure, but at least for ours, there's still always the potential that the actual cost of the test could prove to be a barrier too. Fortunately, that's a manageable problem that you can work to reduce. There's also the danger, we talked about how false positives can make folks actually clog up services in part, but there's not an insignificant psychological cost to thinking you have cancer when you don't, which is always something good to remember. There's definitely workarounds to fix that, but that's always something that we want to keep in mind.

S: For cancer screening, that's something that you have to think about. I guess I didn't think about that as much with our test because, although COVID can be pretty impactful in your life, for most people it's not as serious as something like skin cancer, so a false positive doesn't have as much of a psychological effect. Same thing for most infectious diseases that we would be testing for. I've read recently, I think it's a bit of a topical subject, this idea of overscreening for things like cancer. So I know that there's a lot of emphasis in modern preventative healthcare on screening for cancer, for prostate cancer or breast cancer, getting regular checks, but I think there are some people, some doctors, that say that sometimes overscreening, if you find a tumour, it could end up being a tumour, that if it wasn't causing any symptoms, which I guess it wouldn't if it was caught in just a regular screen, it could be that the treatment for that tumour, which could involve chemotherapy or radiation, a lot of cancer treatments are negatively impactful on your overall health, if that tumour wasn't

causing any symptoms, there's a potential that the treatment for that tumour actually gives you a worse health outcome than just letting the tumour be. So I think that's another thing to think about anytime you're making cancer testing really widely accessible. There could be people that are over testing their own moles. I think that's a difficult subject.

O: On that note, there was also, at least in the US, where we have our unique system of incentives that focuses on making paperwork and charging extra for everything, our setup partially incentivises doctors to biopsy and test for cancers even when it's likely that there isn't going to be a cancer. Part of that is because big private equity companies have been buying up healthcare providers, a lot of private healthcare providers have been closing, and then within that there's been a lot of pressure on private dermatology practices to spend more money. And so even if doctors aren't, like, malevolently "haha, I'm going to test someone for cancer they don't have so I can go out to a fancy dinner," /j there's still that unconscious incentive to, like in the back of their mind, "I need to make more money and so I'm going to be a little more cautious in testing folks." There's always that danger with the test. Fortunately I think we can also structure our tests and use the really cool technologies that both our teams are looking at to address that problem too. If we use things like rapid tests to help people gauge their risk, we could also reduce unnecessary treatments too with lower-cost tests. What our project was looking at, there's about 60% of dermatologists, so a really high number, that say that they will biopsy patients for stuff that they know isn't a melanoma. And part of that, obviously, isn't evil. That's trying to give patients peace of mind, or helping them deal with stuff that's cosmetic. But, part of that is also probably that unconscious incentive to spend more. So if you could take a test inbetween and say "oh no, this mole is fine," for maybe five bucks, then you don't have to spend \$100 getting it removed. Which is, if you really think about it, both our technologies.

J: Yeah, absolutely. I think this really speaks to that wider iGEM idea of human practices. Knowing that we have this world where we can't control how our technology and what we're creating will be implemented, and having to consider these scenarios where you could have all of the people buying up the tests or how we can deal with, or mitigate, what we can't control. We've talked so much today about things that we really can't do anything about. We can't do anything about... Our little tests aren't going to solve the broader issues that we've talked about. We can only consider how they will be applied in their contexts. I guess it's really considering that careful implementation as you said. Picking when and where these tests are going to be available, and who they're going to be available to. That is going to be critical to keep that system streamlined and running.

C: Yeah, and I just wanted to mention, who knows, maybe one day these tests that we've been talking about for the past couple of minutes, maybe they will be picked up and actually turned into something. Which is like the beauty of what we're doing here with iGEM which is really cool.

S: Thanks everyone for coming today, that was a really interesting discussion. I think we both learned a lot about our different countries and our different tests and how those tests could be

applied in those countries. So thanks again for coming and having this interesting discussion. And thanks everyone for listening to our podcast. If you listen to this, you are very dedicated because it's quite long. But hopefully you learned something. What was that Owen?

O: Especially if you listened to the end, we appreciate it.

S: Yes.

J: Yes.

S: Thank you! Bye everyone!

All: Goodbye!