Larry McNicol Module 1 presentation

***Sophie Scott* (Master of Ceremonies)**: Thank you Leigh, that was very insightful and it is amazing to think that it is going to be in Russia and Kazakhstan so that's a great achievement. I would now like to welcome Associate Professor Larry McNicol to discuss Module 1 which covers critical bleeding and massive transfusions. Professor McNicol is the Director of Anaesthesia at Austin Health and the Chairman of the Victorian Consultative Counsel for Anaesthetic Mortality and Morbidity. So please welcome Professor Larry McNicol. [Applause]

Associate Professor Larry McNicol: Thanks very much Sophie, and I was just saying to Daryl and Craig it wasn't far to walk for the three wise monkeys, or not so wise monkeys! I'd just like to thank Leigh and the NBA for getting us to this day. It's been a really long ride. I think those of us that were involved from the outset, many of whom are here today and first met back in March or April 2008 to start this process, and by the time obstetrics and paediatrics modules are complete, hopefully at the end of next year, that's a pretty long haul.

It is an exciting time for us all. With you indulgence I just want to spend a little bit of time, on behalf of the Clinicians involved in the guidelines review, to talk about the process and then I'll just mention a few of the key elements in the Critical Bleeding and Massive Transfusion modules.

The language has changed, a paradigm shift, whatever you like to call it and it's long overdue. Those of us that were involved trying to get some traction for implementation of the previous NHMRC Guidelines were quite frustrated with just getting awareness and knowledge about them, never mind whether they can be implemented. But I think we've come a relatively long way and these, the language of the Patient Blood Management is now are here to stay.

The focus has gone, quiet correctly, from the product which is lifesaving and very therapeutic intervention, but as we have discovered is a hazard as well, it doesn't come without some baggage. So now in the decade between the two sets of guidelines the focus we have gone from the product to the patient, and very appropriately. As Leigh has said, there was quite a few gaps in the previous guidelines, there was nothing on critical bleeding and massive transfusion. There was a sort of scattergun approach to sort of what might be the indications for the various products and certainly nothing about obstetrics and paediatrics. So there has been some gap filling in designing the modules and what we set about doing at the early stage was to construct a set of key research questions that we called the generic questions that we wanted to apply across all the modules. And then for each particular subspecialty modules to design what we thought might be the most important research questions for that specific area. We won't talk about it much today but importantly as well, as well the systematic review process that was very structured, we sought to do some grey literature background research as well, that varied in its volume depending upon the module.

The process, again Leigh alluded to this, I think as one of the people involved that has had a strong interest clinically in transfusion medicine for three decades, this has been one of the most exciting things I have been involved in because of the collaboration, because of the mutual learning. We were devising research questions and sitting down with professional systematic reviewers and

interacting in order to get the literature search on the right path and then evaluate the literature as we went through.

Those of you, and there are many here today, who are very experienced researchers and they are aware about the robustness of the processes that need to be put in place if you are going to make recommendations. And Transfusion Medicine has been relatively bereft of science for a long time compared with a lot of other areas of medicine. So we were not anticipating enormous amount of scientific evidence but perhaps that made it even more important to undertake this in a very structured way.

So the modules will only contain recommendations where there was sufficient evidence from the systematic review. But even then, and with a lot of help from expert medical writers as well as those that wanted to get their clinical points across, we needed to make sure we used the language very clearly.

Again, pretty important rules of engagement the NHMRC levels of evidence, that when you look through the guidelines you are not going to see too many A's! There's a few B's, and there's a few C's and D's but there is also a lot of practice points. And again, this is not people sitting around a room saying "I'm an expert lets tell people what they should do". We felt once we had looked at the literature that it was also important to provide some guidance for Clinicians in an area that is very challenging. So the practice points, and there are a lot of them, again were felt to be an important part of the guidelines.

Just to go now very briefly to a few elements in the first module. The literature in this whole field has struggled because of lack of clarity about definitions. So we spent quite a few hours first of all, trying to decide what we thought was reasonable definition of critical bleeding and massive transfusion, in order to inform the systematic review about what we were looking for. And this is one of the generic questions applied to this population [*In patients with critical bleeding requiring massive transfusion, what is the effect of RBC transfusions on patient outcomes?*] and it's an important one because all of us involved in this field know that over the last decade in particular, there is emerging evidence that to have a red blood cell transfusion that may be lifesaving may also be doing harm, so it's a fine line.

So on that question, we don't have high level of scientific evidence. We just need to recognise in practice points, what's important to help clinicians understand. We all know if you deny someone access to blood when they have had a massive injury or they are bleeding from an obstetric haemorrhage or in another situation, they will die, they need it to save their life. But there is enough evidence to say that the more you give in that situation the bigger price you might pay. So the way to do that is to use a protocolised approach. And the implementation of a massive transfusion protocol is a key element to this modules outcome.

Just briefly with Helen Savoia and some others including James Isbister who is in the audience today, we were in Melbourne last week at a Transfusion Outcome Research Collaborative whole day talk on Obstetrics haemorrhage, which is terrific timing given the launch of work in the Obstetric module. But Euan Wallis is Professor of Obstetrics at Monash, referred to the massive transfusion protocol in his hospital as the thing of joy, the thing of beauty! He was so impressed at with how their whole behaviours had changed because of the protocol.

Now one of the other key questions in this field, and this is where clinicians have been voting with their feet before the evidence is necessarily there. Everybody talks about ratios, and the desire to maybe give early FFP and perhaps platelets to switch off the coagulopathy that might be associated with certain types of massive haemorrhage, particularly trauma and probably particularly obstetrics. When we looked at the literature, so though with this particular question, the only thing we found was that what you needed is to have a massive transfusion protocol, and in that you can include advice about the ratio of blood component therapy. But the evidence is such that, and again note here it is only grade C, that what you needed to improve outcome is to have the protocol, not to get hung-up on your ratios. And so practice points that fall out of that systematic review tell us that we weren't able to find anything that said this is the ratio that you need. Even though a lot of our consumers, which are clinicians, wanted us to be able to say "yeah, give two to one, or one to one to one all the way through" there isn't the evidence for that even though there are some papers in trauma literature that might suggest it. What matters is having the protocol!

We were also probably had some disappointment from people when this module first rolled out about was there a magic bullet in the form of activated recombinant VIIa. We've all used it, we've had patients' lives who we think might have been saved by it in various situations but the evidence is not there for it to be routinely used as part of an MTP. There will be some patients where you probably can, when you have done everything else maybe salvage them.

So the key message for this module is we've offered a template for a Massive Transfusion Protocol. We recommend that institutions— all of which have different resources and different questions, to adapt it to their local needs. And again it includes, without apology, a lot of common sense clinical advice that again is driven by our literature search, our systematic review. But hopefully it is also the sort of thing that can if it is adhered to genuinely improve patient outcomes.

Just very briefly, one thing that is in there is tranexamic acid. There was a big trial on tranexamic acid called the CRASH-2 Study that was in trauma populations. It wasn't published until after the deadline for this module and our systematic review and importantly as well it was a different patient population, it was an all comers trauma population. But it was a very compelling trial and so the improvement in outcome in large, international, well researched, well structured trial was that Tranexamic acid improved … [Video skips at this point]commonsense said it should be in there.

As well as having an MTP, there needs to be some advice about other elements to managing the critically bleeding patient and that's in the guidelines as well. And it is important as well, and this came through as well in the obstetrics meeting last week. Is that those of us that are at the coalface and are pouring in the blood products sometimes forget the people in the lab who have gone the extra mile to provide the product and so knowing when to stop the MTP so that everyone can say well done, the patient is going well, thanks for your help. And again, another example of the enormous collaboration.

I'd just like to finish by expressing my appreciation for being involved but also there've been an enormous number of people. But I would just like to mention three people from my perspective from the time I have been involved. Two of them are clinicians, and one of them is going to speak to you later on, Craig French and he with Amanda Thompson as haematologist from Sydney, have been the co-chairs of the Expert Working Group right from the start, their going to see it right through. Their leadership and dedication has been a key factor in the success of this module. So I am really

sorry that Amanda couldn't be here today. And Jen Roberts, who Leigh mentioned has been the absolute driver at the NBA, that's kept us all on our toes, kept us focused when we'd be wandering off into the mist of our own importance. And so again I regret that Jen's not able to be here but I wanted to mention her enormous contribution. Thank you very much.