Questions I wish the doctors would answer May 2021

I have been asked “what am I trying to accomplish?”
Why cannot I just trust the doctors?
Its not about trust; its two fold

1: I have concerns about the organizational structure of hospitals and how they solve problems, this comes from my training discussed elsewhere on www.what-beleive.ca in the PDF “what am I trying to accomplish . PDF”.

This is not my problem other than the current structure on one level failed me and I have the expertise and training to pinpoint exactly why it happened and the way it happened. For my mental health I had to document what I experienced, as documentation is a part of process control.

2: Their is also a history here;
-My Great Grandmother died of Uremia in 1923 after a kidney was removed, PKD?
-My Grandfather died of a heart attack in 1945 at 58, probably PKD.
-My mother had PKD and lived to her 80’s but an uncle of mine died at 60 from PKD, he could not face 1975 era treatment and did nothing.
-I have PKD, it reared its head when I was 58, dialysis and a transplant! That makes me the lucky one and I am very aware and grateful.
-I have a brother and children and nieces with PKD and I have grandchildren.

Look at the progress in medical treatment from my great grandmother (1923), to my grandfather (1945), to my uncle (1975), to me (2015) and I can see the direction things are going for my children, the new drugs, the talk of turning off the genes, I am thrilled at the progress.

From what I know about process control and capability maturity I know there is so much more that can be done, I know the changes will happen with or without me, but if I can make a contribution to my local situation, and survive, then I am just another experiment that makes my children s life a little better and a little longer.

I was negligent in how I understood my situation, pre transplant. Having been blessed with a kidney I now have a responsibility to know as much as I can for the next phase of my totally awesome kidney adventure and whatever fortune befalls me.

My apologies in advance if you perceive my questions as anything other than trying to understand the situation so that my children will not be as uninformed as I was.

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	Questions about my Understanding of my situation?
A	Is my math about the risk correct? On the cancer.org website I read the risk of getting a lymphoma at 1/417 for the general population, calculated it to 1/139 for the transplant population and calculated it to 1/55 for my situation with my serology status change post transplant. Is my understanding of the risk correct?
B	I have read about the complexity of different lymphomas. Is Post Transplant lympho proliferative disease a distinct disease or is it just NHL and HL that occurs after transplant when you are immune suppressed. Is it the same diseases, just more aggressive because of the required immune suppressants?
C-1	Is there something about my condition that made you disregard the risk of cancer in favour of a transplant, the difference in hazard ratio between dialysis and transplant and EBV transplant and PTLD indicates there must have been some over riding consideration to give me this particular kidney, what was that consideration?
C-2	When a doctor make a diagnosis does he or she; A: diagnosis from his education and experience, or B: follow a process -specific protocols defined for each group of symptoms or suspected diagnosis -tests confirm the diagnosis -a previously agreed to treatment plan based upon research is performed, that research is constantly updated into an agreed to “data-set” that the doctor and others draws upon. -The real work of the doctor is updating the data-set and working with his or her colleagues to develop a consensus on treatment and then use the data-set consistently. -if there is a failure, research is initiated into why the failure occurred. -once the root cause of a failure is understood, the process and data-set is updated -an improvement in outcome is noted; if not repeat research and updating of data-set with new clinical research.
D	Valganciclovir was given to me for 3 months after transplant. Was that due to the increase risk of PTLD from the kidney with EBV. The literature talks about it as a prophylactic, at the time I was told its just something you are doing to all patients, was that a pat on the head, do not worry kind of statement, or was the drug you were giving me specifically to address my increased risk from the serology mismatch.
E	I read about a hospital in Alberta (the reference escapes me) that did preemptive Valganciclovir treatments to scheduled living kidney transplants. Is it possible to do the same for people who were in my situation. Once a person gets close to the top of the list, start prophylactic Valganciclovir, or is that impractical and dangerous?
F	My first 3 months were very difficult, if I remember correctly it was also when I was on Valganciclovir, was my reaction to it or the other meds, is the harshness of this drug why you are cautious in its use, specifically referring to question E?
G	Dr Zimmerman rejected the first kidney it was an Expanded Criteria Donor (ECD) kidney due to age. It was rejected before I even was informed of the availability. I found a fact sheet that explained the types of kidneys. In anothers handwriting were explanations, the ECD were crossed out as were the HSP, as I am not highly sensitized, but the ExD was checked. So at

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	some point a discussion took place, the ECD was decided to be rejected and the ExD was decided to be accepted. I only know of this because I kept the sheets. I have no recollection. Q: Was the exceptional distribution donor (ExD) of the kidney offering a seropositive kidney to a sero negative patient? Q: Was the exceptional nature of the kidney the possible Aids exposure of the partner 20 years previous, or the death of the donor from cancer? If so what was the actual risk?
H-1	If I am correct in my reading comprehension; there is a risk due to mis matched EBV serology; Who was the doctor who reviewed my file, and the donated kidney and said yes this is good to go? Did this doctor think my risk was 1% or did he/she understand that the risk was much greater? If not has their been any corrective actions?
H-2	Do you see the serology mismatch as a problem in the decision making process?
H-3	Is there a decision making process?
H-4	Finally I get to decide, but who warns of extreme danger? When does a high risk transplant become inadvisable and whose call is that?
G-1	A fellow during a clinic visit (pre covid) quoted the 1% risk of EBV to me, he became quite agitated when I suggested he was not familiar with the literature on the subject when discussing EBV and PTLD. Today, knowing what I know, I would admonish him and send him out of the room and ask to speak to a competent physician. At the time I was sick and easily intimidated. I now know that the risk of PTLD is a function of my EBV level, acknowledging that 1/3 of PTLD's are not a function of EBV level. If I was talking to that same fellow today would the messaging be the same; that the risk of EBV and PTLD after transplant was 1% when serology was mismatched?
G-2	If you were to call a EBV- serology patient today with an EBV+ kidney would they be told, it was a 1% risk of EBV and it was only a slight adjustment of the meds to fix things up or would they be told by accepting the EBV- kidney they had a 1/11 chance of getting a lymphoma that is often described as the most serious complication of a kidney transplant? Has the messaging changed in the last year?
G-3	Would it make a difference who was calling the patient, in regards to the message they receive in terms of the risk?
H-1	I get a once a month EBV blood work and you are watching, I appreciate the effort. Thank you. I have been told the trigger is symptoms, like night sweats, weight loss, I have also read that the trigger is EBV viral load >10,000 copies/µg DNA; Rapid increase in EBV viral load; EBV viremia plus presence of B symptoms; Positive CT scan; Positive biopsy. My EBV viral load has been above 10,000 and has fluctuated rapidly and I have been referred to Dr Buchan. Is every pre PTLD patient sent to her, out of nephrology.
H-2	What is the trigger that leads to pro active treatment -reduction in immune suppression, -rimuxlab -EBV-CTL immunotherapy; pending question about serology problems

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H-3	Do the doctors at the hospital have clinical experience in EBV- to EBV+ PTLD post kidney transplantation?
H-4	If yes, what have the outcomes been for other patients in my situation, can you provide me any insight. I appreciate that you cannot predict the future, it would be helpful to know that someone has this covered, has seen this before and has some success.
i-1	Having kept cattle I think about them as a metaphor for life. Its really hard to get the first cow on a trailer, but the second cow goes on easily because he is following the first and the third just walks on, I suspect they enjoy the ride, the air is fresh, they are zipping along the highway. They are oblivious to their final destination, and despite the vegan rhetoric to the contrary right up to the last minute, everyone tries to keep them calm and happy, they weight about 2000 pounds and have to want to go where they go, they do have a choice. I feel the transplant was a bit like that. Make no mistake I am better today than when I am on dialysis, but it has been a hell of a trailer ride. I am expected to make the final decision about "getting on the trailer" or what treatment I am fortunate enough to get or not accept, but to make the decision I need to be informed. To be informed I need to be educated by people who have experience. If I am not making an informed decision I might as well be a cow getting on a trailer for his trip to the "big farm" This question deals **partly** with my perception. Q: Why am I being treated like a cow going to slaughter?
i-2	Is my expectation of having answers from doctors with experience in my condition unreasonable?
i-3	It was explained to me by one junior doctor that no senior doctor has taken an interest in my rare disease and that is why I never talk to a senior nephrologist. Is this true?
J	I have read that outcomes from HL and NHL are 70% survival 10 years out. That makes me very optimistic about my odds, 70% chance of surviving a 1/10 chance of getting. In the rimuxlab era for a 64 year old transplant patient what are the odds?
K-1	I have read their are 4 classes of immune suppressant maintenance drugs: • Calcineurin Inhibitors: Tacrolimus and Cyclosporine • Antiproliferative agents: Mycophenolate Mofetil, Mycophenolate Sodium and Azathioprine • mTOR inhibitor: Sirolimus • Steroids: Prednisone [i] I was on Tacrolimus, Azathioprine and Prednisone. To give my immune system a chance to fight off the EBV my anti rejection was reduced. I am no longer on the Antiprolefertive Azathiprine, My layman understanding is that I am at risk for a highly proliferative type of lymphoma (PTLD) and I am not on an anti proliferative.

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	I see the word proliferative in PTLD, and think to myself, an antiproliferative might be a good thing. Should this be a cause for concern? Are their any studies, case reports, lacking that specialists anywhere online that have a hunch to indicate the best combination of anti rejection drugs for a person in my condition EBV- to EBV+ with Chronic EBV? My interest is in saving the kidney (we have become attached) and avoid PTLD, NHL and or HL (I could happily spend the rest of my life not knowing any more about cancer.)
K-2	Have you seen any subtle signs of rejection?
K-3	Is it possible to go back on the full spectrum of anti rejection drugs? Would that even be beneficial?
K-4	The first three months after transplant were difficult. A few different drug combinations were tried. Reflecting back on it and reviewing my notes I am suspicious that the worst reactions were due to the anti viral. Comments or clarification would be appreciated.
K-5	If K-4 is true, is there a better combination of anti rejection drugs for me today, post anti viral?
	These questions deal with my current health situation.
L	How am I doing? I have not had a serious discussion with a senior nephrologist in about a year, I am curious about my condition.
M	I do not have cancer now. I can tell by looking at my blood WBC and RBC counts. Is that a correct understanding.
N	Just an FYI, I am feeling much better with increased endurance in my walking lately. My progress has been incredibly slow, what level of activity can I expect based on your observations of literally a thousand other transplants. Lets put me in the 9/10 who do not get cancer, how active could I become if I keep pushing it?
O	On the off chance some doctor in nephrology does read this, I want you to know I am grateful and very happy. What you did to me is an absolute miracle, I should be dead but I am alive and enjoying my children, grandchildren, my sweetheart, my garden, my farm at a level I could not do while on dialysis. My activity level is increasing, ever so slowly. I see constant improvement. So thank you. Not a question, I just want to make sure you understand. Sometimes I am just a bit on the nose.
1	**These questions are specific to post PTLD treatments**
2	A 2018 study stated that EBV-CTL immunotherapy targets PTLD. One center experimenting

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	with allogeneic, third-party EBV-CTL for the treatment of PTLD in SOT patients achieved an overall remission rate of 80% (8 of 10). Should I develop PTLD is this a viable treatment?[ii]
3	In this 2002 study they stated "standard protocols are not effective in generating CTL from **seronegative recipients** of EBV-carrying organs, who are the patients most at risk for the development of EBV-LPD. For CTL to be an option for the management of EBV in these patients, a sensitive and specific assay for the prediction of high-risk patients is required as well as an effective method for the generation of EBV-specific CTL from seronegative recipients. [iii] Q: Has this problem been overcome in the ensuing 19 years? Q: Can the outcomes of EBV-CTL immunotherapy that targets PTLD be expected as stated in question 2, which is from a 2018 study?
4	Is a 2005 combined chemo immunotherapy regimen including virus-specific T-cells an effective first-line treatment of EBV-related PTLD? [iv]
4.1	In this 2005 experiment all patients showed a complete response to treatment, without therapy-related toxicity or rejection, and persist in remission with good renal function at a median follow-up of 31 months.
4.2	The authors state the treatment of EBV-associated post-transplant lymphoproliferative disease (PTLD) poses a considerable challenge. Q: What is the challenge? Q: Is Dr Buchan or others consulting with people actively working on this challenge? Q: Can you refer me via electronic communication to who ever, where ever these discussions are taking place
4.3	"Efforts have been made to define regimens based on combination of the available therapeutic agents, chosen and tailored on a patient-by-patient basis, with the aim of augmenting event-free patient and graft survival" Q: What are the therapeutic variables "on a patient by patient basis"? Q: I do not know the technical term but can you consult with these people, set up a dialogue, copy their notes, cheat on my behalf? Q: Is there a "PTLD doctor forum"?
4.4	Is there one doctor or hospital, university, clinic, drug company, that is specifically and single minded in terms of PTLD?
5	An older study called for the use of rituximab in preventing PTLD among patients with primary EBV infection. Is this considered effective and safe are there newer studies? [v]
6	In Dec 2000 in Lymphoproliferative disease post-renal transplant[vi] Charles G. Newstead made the following conclusions
6.1	"the primary infection that is seen in a seronegative recipient of a seropositive graft is an important risk factor for PTLD with a relative risk factor of 76 fold increase in that situation;" Given that the hospital is engaged in "Exceptional Distribution Donor" (ExD) i.e. "a kidney donor who is at an increase medical risk of transmitting an infection or cancer." quoted from non controlled document "different types of donors dated January 2016" Given that 20 years ago that Newstead recommended "The development of a database to

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	properly assess the value of novel therapeutic approaches will not be easy given the small number of patients involved, and is likely to require a collaborative effort between transplant centres in more than one country. Q: Did anyone who approved risky transplants reflect upon, act upon, or aware of this 20 year old recommendation? Q: As the patient "decides whether to accept or decline the offer…" of a ExD kidney, do you expect the patient to be aware of the specific risks, recommended action plans laid out 20 years previous, and was I as a patient expected to know and contradict the incorrect information when staff were were offering me the kidney?
6.2	In the first line of Newsteads study he states "The incidence of post-transplant lymphoproliferative disease (PTLD) in renal transplant recipients is of the order of 1%" This is the disinformation that I was told. He then goes on to talk about the adjustment of drugs that would be required in the event of PTLD, alluding to what I was told. He then goes on "The primary infection that is seen in a sero-negative recipient of a sero-positive graft is an important risk factor for PTLD with a relative risk ratio of 76-fold increased in that situation; " ….the primary risk is in pediatric patients. I was given incorrect information, I have been chastised and belittled by a doctor for correcting his ignorance in citing 20 year old literature. Q: is this 20 years old study valid or is a quack study from a vanity press? Q: Is there anyone at the hospital who cares about this? By "this" I mean either sharing my obvious concern or perhaps a concern for my mental health?
6.3	Q: Am I suffering from some sort of paranoid delusion? I see this as a colossal blunder, can a senior nephrologist look me in the eye and say a 76 fold increase is not significant? Q: I have been seeing a staff psychiatrist Dr Green. Does he think I am clinically insane to be concerned about this situation? Q: Do the nephrologist think I am just a "cranky bitch" who likes to make noise and feels sorry for himself?
6.4	Is Nephrology Dialysis Transplantation a publishing mill, or is it a valid peer reviewed journal? *"Nephrology Dialysis Transplantation: an international basic science and clinical renal journal (ndt) is the leading nephrology journal in Europe and renowned worldwide, devoted to original clinical and laboratory research in nephrology, dialysis and transplantation. ndt is an official journal of the ERA-EDTA (European Renal Association-European Dialysis and Transplant Association). Published monthly, the journal provides an essential resource for researchers and clinicians throughout the world. All research articles in this journal have undergone peer review."* https://academic.oup.com/ndt/pages/About

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