Integrating functional testing into your clinical routine

From dipping your toe…. to the deeper dive

Louise Carder, BSc Nutr. Med., Pg. Dip., mNNA, CNHC Reg., IFMCP, mBSEM, mNAP

About Louise

Nutritional Therapist and Director

- BSc Nutritional Medicine (with previous BA (hons) & Pg. Dip.)
- mNNA, CNHC Reg., (previous Director & Head of Communications at BANT)
- IFMCP
- Co-author of Integrated Approaches to Infertility, IVF and Recurrent Miscarriage (published 2015 by Singing Dragon), as well as a multitude of articles
- Only Shoemaker Certified Practitioner in Europe
- Bredesen Protocol trained practitioner (2017)
- Passionate health practitioner with 15 years of clinical practice experience
- Qualified Venipuncturist
- Founder of Colab Services Ltd
- and a Mum…..

A passion for knowledge

“Real knowledge is to know the extent of one’s ignorance”

Confucious

Need For Testing

“ 70% of clinical decisions rely on laboratory testing”

Hallmark, Mike J. The 70% claim: what’s the evidence base? Ann Clin. Biochem 2011; 48:487-8

Need For Testing

“ The original data from the Mayo Clinic stated that the relative amount of data on the Mayo Electronic Result Enquiry System was: pathology: 94%, radiology: 3%, **patient data: 1%**, electrocardiogram: 1% and surgery: 1%”

Hallmark, Mike J. The 70% claim: what’s the evidence base? Ann Clin. Biochem 2011; 48:487-8

Need For Testing

To go back to the 70% claim, recent studies from the US and Germany have found 60-70% of clinical decisions were affected by laboratory test results, both in the hospital setting and outside

Rohr UP, Binder C, Dieterle T, Giusti F, Messina CG, Toerien E, et al. The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report. PLoS One 2016;11:e0149856

Sikaris KA Enhancing the Clinical Value of Medical Laboratory Testing. David Curnow Plenary Lecture, Australian Association of Clinical Biochemists Annual Scientific Meeting 2016 accessed https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759162/pdf/cbr-38-107.pdf

Where do we go from here?

RESEARCH Open Access

A theoretical model of health management using data-driven decision-making: the future of precision medicine and health

Eva Kriegova[1†], Milos Kudelka[2†], Martin Radvansky[2] and Jiri Gallo[3,4*]

Abstract

Background: The burden of chronic and societal diseases is affected by many risk factors that can change over time. The minimalisation of disease-associated risk factors may contribute to long-term health. Therefore, new data-driven health management should be used in clinical decision-making in order to minimise future individual risks of disease and adverse health effects.

Methods: We aimed to develop a health trajectories (HT) management methodology based on electronic health records (EHR) and analysing overlapping groups of patients who share a similar risk of developing a particular disease or experiencing specific adverse health effects. Formal concept analysis (FCA) was applied to identify and visualise overlapping patient groups, as well as for decision-making. To demonstrate its capabilities, the theoretical model presented uses genuine data from a local total knee arthroplasty (TKA) register (a total of 1885 patients) and shows the influence of step by step changes in five lifestyle factors (BMI, smoking, activity, sports and long-distance walking) on the risk of early reoperation after TKA.

Results: The theoretical model of HT management demonstrates the potential of using EHR data to make data-driven recommendations to support both patients' and physicians' decision-making. The model example developed from the TKA register acts as a clinical decision-making tool, built to show surgeons and patients the likelihood of early reoperation after TKA and how the likelihood changes when factors are modified. The presented data-driven tool suits an individualised approach to health management because it quantifies the impact of various combinations of factors on the early reoperation rate after TKA and shows alternative combinations of factors that may change the reoperation risk.

Conclusion: This theoretical model introduces future HT management as an understandable way of conceiving patients' futures with a view to positively (or negatively) changing their behaviour. The model's ability to influence beneficial health care decision-making to improve patient outcomes should be proved using various real-world data

Where do we go from here?

1. Data describing the patient's current condition reported as a set of factors in their EHR
2. Data representing the patient's history, which is (or should be) included in the EHR, such as the patient's initial condition and its changes over the time preceding their current condition.
3. Data is related to a description of the patient's specific living conditions and their future changes, which are not included in the EHR.

Where do we go from here?

A recent study on Chat GPT by Mass General Brigham has shown that overall Chat GPT was 72% accurate and in making a final diagnosis it was 77% accurate. However, it was lowest, at 60% in accurately making differential diagnoses and 68% accurate in clinical management decisions e.g. treatment path.

Adding value (cost vs value)

4 key purposes of laboratory testing:
1. Identifying signs of nutrient deficiencies/excess
2. Detecting changes in health
3. Evaluation of body function e.g. organs such as kidney, liver, heart, thyroid
4. Monitoring- either treatment/therapy or progression of disease

Rohr's study states "appropriate testing allows early-stage interventions, reducing late stage healthcare expenditure"

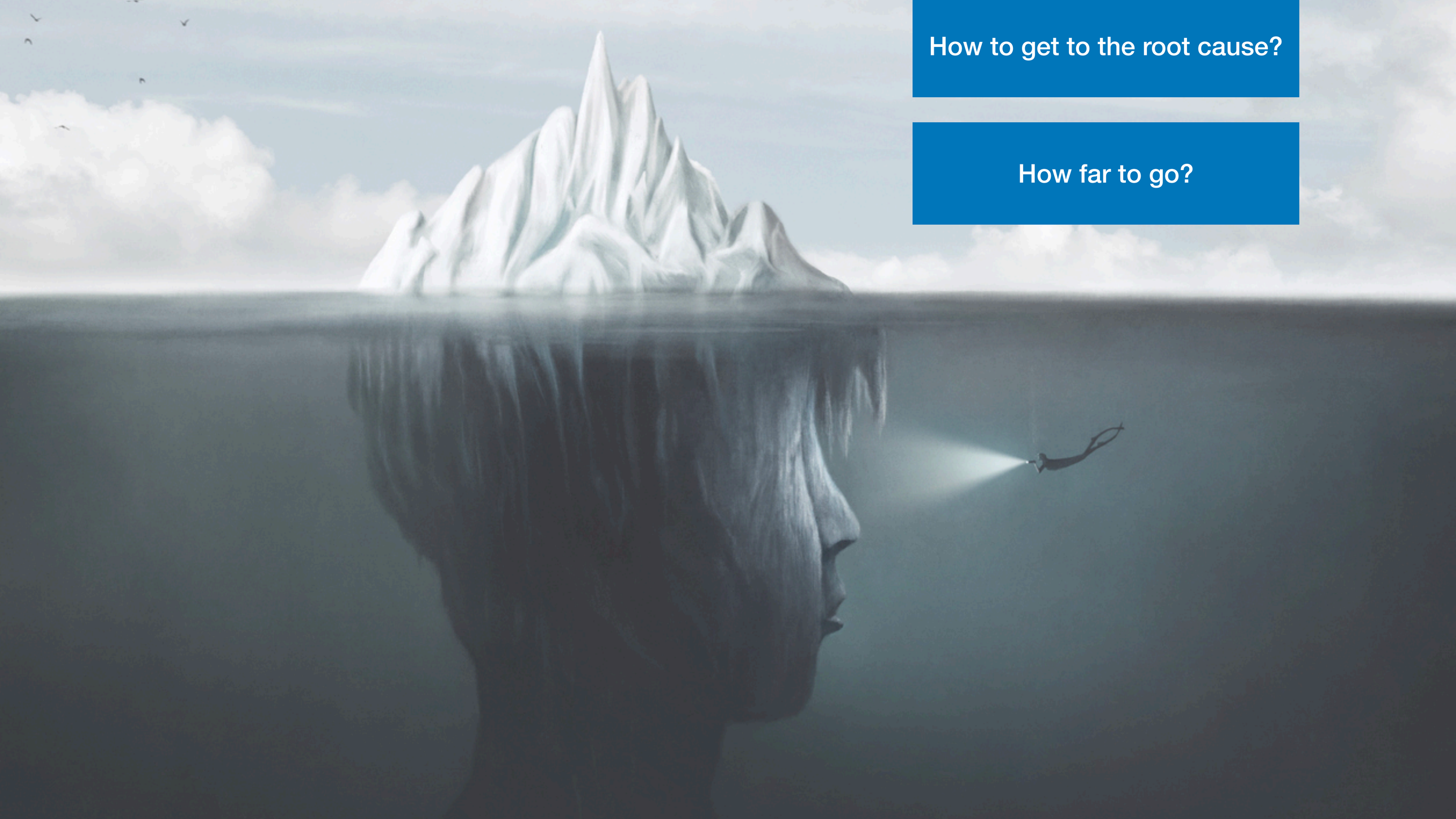
Rohr UP, Binder C, Dieterle T, Giusti F, Messina CG, Toerien E, et al. The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report. PLoS One 2016;11:e0149856

Adding value (cost vs value)

How do we assess value of this? In terms of:
‘Disease prevention, early detection? Accurate diagnosis, treatment selection, minimising delays in treatment, supporting recovery, reducing disability, prevent relapse, slowing disease progression, reducing long term care needs?’

A detailed study by the Lewin Group for the Centers for Disease Control and Prevention in the USA concluded ‘Laboratory medicine is an essential element of the health care system. It is integral to many clinical decisions, providing physicians, nurses, and other health care providers with often pivotal information for the prevention, diagnosis, treatment and management of disease’

The Value of Laboratory Medicine to Health Care. Chapter 1. In: *The Lewin Group: Laboratory Medicine – A National Status Report*. May 2008:19–65.


How to get to the root cause?
How far to go?

Going too far?

For higher order differential diagnostic reasoning, careful attention should be applied to:

(1) how test metrics can be misleading

(2) how diagnostic labels may overcomplicate care

(3) how using different methods of classifying diagnoses could improve management

Cook CE, Décary S. Higher order thinking about differential diagnosis. Braz J Phys Ther. 2020 Jan-Feb;24(1):1-7.

Integrating Functional Testing

Considering the journey from initial integration of functional testing into a clinic routine

What this means for the practitioner and what the patient should also consider

Integrating functional testing into your practice

1. What test and when? Practitioner perspective

a. Existing tests, perhaps even a sequence of tests- where are the gaps?
b. Do you need a foundation level result early on to then track?
c. Do you need a client to stop taking any medication/nutraceutical or do you just want to assess where they are at right now? (This can affect timing of a test)
d.What testing method you you want to use? There can be options e.g. Zonulin: stool, blood level, antibodies
e.When can the client provide the sample e.g. cycle, draw location etc
f.Which lab are you going to use? e.g. test type, price, service
g. Which lab facilitation service are you going to use? e.g. shipping
h. How educated you feel/tech support on offer- do you have a sample report to chat through with the client?
i. Is the test covered by your professional practice insurance?
j. Has the client signed a consent to testing?

Integrating functional testing into your practice

1. What test and when? Patient perspective.

You need to know:

a. What information you are going to get and how this will inform next steps. Can be useful to ask to see a sample report

b. What the price is and what any other options might be, so asking for comparisons can be useful

c. What the commitment is to achieve a sample e.g. will a blood draw be required and how would you get that done & does the kit have any contents you need to do something with once it arrives? Will timing be a factor in producing a sample?

d.What are the next steps likely to be? How much will that cost?

e. Will the test need to be repeated? If so how will this be decided & when?

f. That you are absolutely happy with the test & have signed a consent form with your practitioner

Integrating functional testing into your practice

2. What do you need to know about the process? Practitioner perspective

a. Does the patient have all the information they need to feel comfortable with their decision, costs etc.

b. Are you happy with how to order the test itself? How it is dispatched, what the client has to do to achieve a sample? Can you answer all the questions from the patient perspective on the next page?

c. Are you going to hold the kits in stock or order in each time? (If holding them do check expiration dates)

d. Do you charge an interpretation fee for tests or do you have the client pay the RRP for a test and get commission? Time has to be accounted for ordering/interpreting the test so it is important to make a decision on how you are going to account for it.

e. Have you a way of scheduling in the client's results appointment for a rough date of when the result will be back, and what prep work will need to be scheduled in too in order to review the result/write up a report?

Integrating functional testing into your practice

2. What do you need to know about the test process? Patient Perspective

a. Is there anyone you can call to ask questions once you have the kit? (Practitioner/kit service)
b. If there is a delay to the kit arriving, or the wrong kit arrives, what do you do?
c. If there is anything you need to do once the kit arrives
d. How the sample is going to get to the lab; will a courier collect or do you need to post the sample? Who do you need to notify if a courier is collecting that the sample is ready, or the collection needs to be booked in?
e. When will the results be back? How will you be notified
f. Does the practitioner charge an interpretation fee or is this included in the cost of the test?
g. What kind of interpretation will you receive? Verbal during an appointment or written report?
h. When/how is a results appointment arranged?

Integrating functional testing into your practice

3. What are you going to do with what you find out from the test result? Practitioner perspective

Results have a 2-fold dynamic: 1. The result itself 2. The actions that come from the result

1. The result itself

a. Give yourself time to review and interpret the result firstly- it is important to be able to relay the results to the client with clarity

b. Create a results crib sheet for yourself and build that up over time to refer to so you have a good working library

c. If it is the first time you have run a test, set up a tech. support call with the lab or facilitation service

d. Seek out more education while you are waiting for the result to come back in- check the facilitation service or lab website, to top up existing knowledge

e. Create an action plan crib sheet so you have a baseline action plan ready to go so you're not starting from scratch each time

Integrating functional testing into your practice

3. What are you going to do with what you find out from the test result? Practitioner perspective

2. The actions that come from the result

a. Be clear about the programme you are recommending as a result of the test result e.g. diet/lifestyle/nutraceuticals/medication

b. Be clear about what tracking/repeat testing is going to be required based on the result

c. Is anyone else affected by the result, and what might their actions be? e.g. infection related

d. Is any further testing required? What does that look like?

Integrating functional testing into your practice

3. What might the patient want to know about what is coming next once they have the results? Patient perspective

Results have that 2-fold dynamic: 1. The result itself 2. The actions that come from the result

1. The result itself

a.What do the results mean ie. Individual markers?

b. Can they be contextualised by the practitioner?

c. What is the overarching story of the results

d. Do the results deliver what was expected? If not, why not?

Integrating functional testing into your practice

3. What might the patient want to know about what is coming next once they have the results? Patient perspective

Results have that 2-fold dynamic: 1. The result itself 2. The actions that come from the result

2. The actions that come from the result

a.What is the clear plan of action?

b. How long will it go on for, and how might it change over time?

c. How will you know when any changes might need to be made?

d. Is any further testing required?

e. What about a repeat test plan?

Developing a clinical specialism

The Deeper dive of more in-depth testing

When you have a grasp of the basics then you may want to develop a clinic specialism

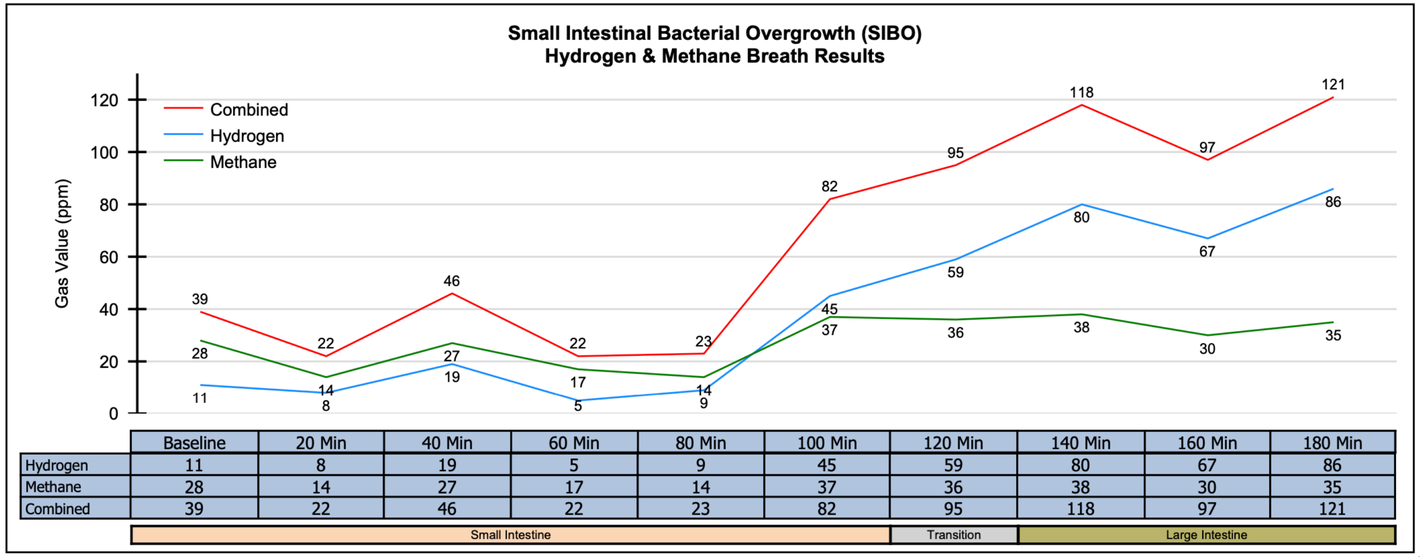
Example: Gastrointestinal Health

SIBO BREATH TEST (LACTULOSE AND GLUCOSE)
Assessment for SIBO; glucose for proximal and lactulose for distal.

FRUCTOSE, LACTOSE AND SUCROSE INTOLERANCE
Assessment for dietary intolerance associated with GI symptoms.

STEP 1 - SPECIFIC TESTING FOR POTENTIAL PATHOGENS GI MAP (+ ZONULIN, + GLUTEN PEPTIDE)
Assessment of bacteria, viruses, yeasts, protozoa, worms and intestinal health test is DNA-PCR so is super-sensitive for identification of H.pylori and other GI species.

PARASITE PANEL
Assessment of parasites from all 7 continents, as well as flukes, yeasts and other significant GI molecules.



	Baseline	20 Min	40 Min	60 Min	80 Min	100 Min	120 Min	140 Min	160 Min	180 Min
Hydrogen	11	8	19	5	9	45	59	80	67	86
Methane	28	14	27	17	14	37	36	38	30	35
Combined	39	22	46	22	23	82	95	118	97	121
	Small Intestine						Transition	Large Intestine		

Developing a clinical specialism

Example: Gastrointestinal Health….. A deeper dive

IN DEPTH MICROBIOME TEST

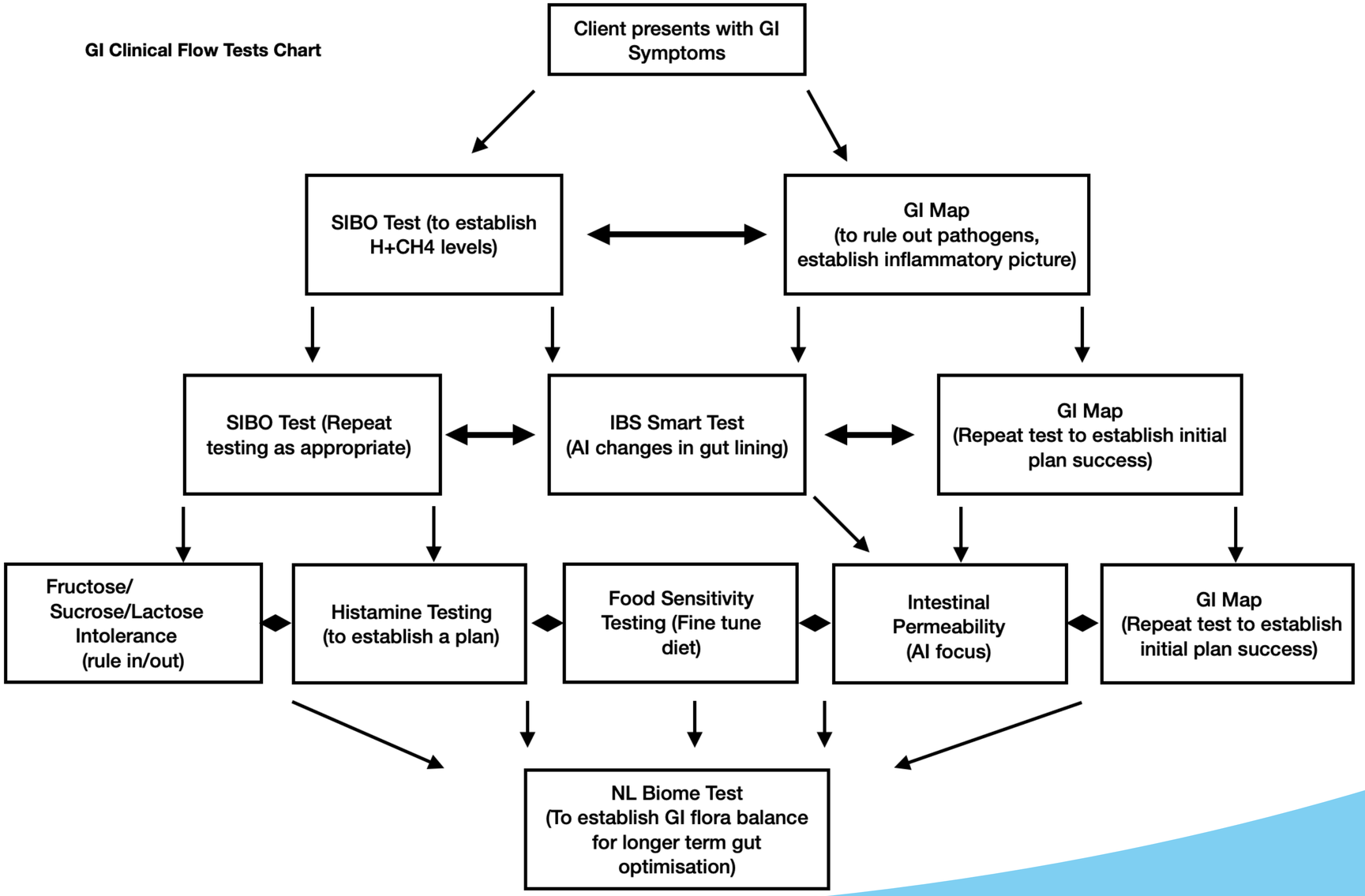
This specialised test considers microbiome composition for a comprehensive GI Microbiome analysis. Not only are individual microbes assessed but a composition graph gives relative percentages of each species. Charts are then provided to show whether levels fall below or are reported above reference values. The result also shows activity of each group with active/inactive percentages given.

IBS SMART TEST

Consideration of antibodies to Anti CDtB and Anti vinculin antibodies, thereby reporting on response to CDtB toxin and development of gut lining autoimmunity

Antibody Detected	Patient Value (OD)	Antibody Levels
Anti-CdtB Ab	1.71	Elevated
Anti-Vinculin Ab	1.17	Not Elevated

Developing a clinical specialism



Developing a clinical specialism

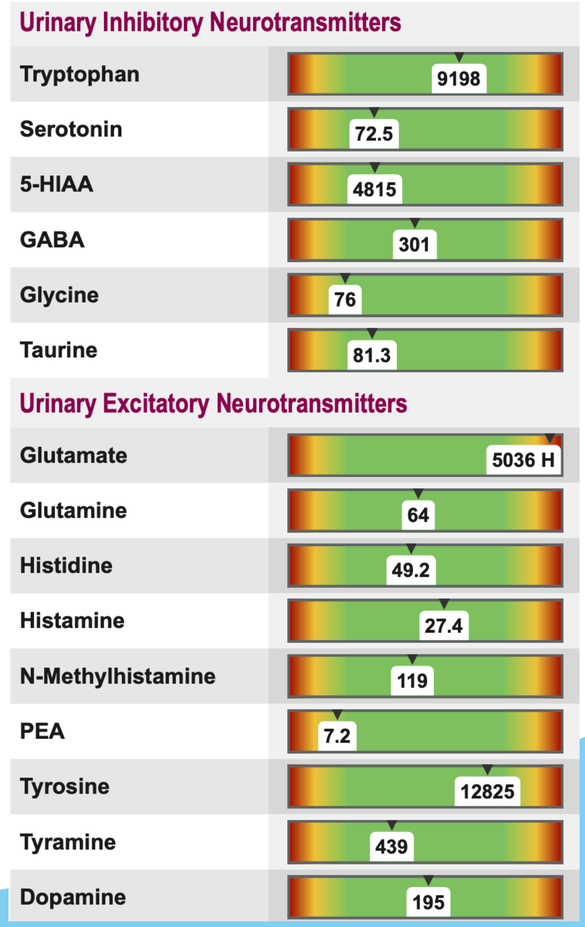
The Deeper dive of more in-depth testing
When you have a grasp of the basics then you may want to develop a clinic specialism

Example: Neurological Health

NEUROTRANSMITTERS
Assessment of biochemistry of neurochemicals to help identify root cause of persistent symptoms e.g. mood disorders.

KRYPTOPYRROLES TESTING
Assessment of Kryptopyrroles which can reduce levels of B6 & zinc.

PRODROMESCAN
Assessment of key body system processes. Systems supported by this test are related to fatigue/mitochondrial health, cholesterol changes, essential fatty acid status and cognitive function through testing Phospholipids, Fatty acids, GTAs, Iron, Choline, Mito function, C-RP, Elongase 5, Peroxisomal function, Cholesterol and Kidney function



Developing a clinical specialism

Example: Neurological Health: A deeper dive into cognitive decline

PRECODE PANEL AND 6 + 12 MONTH REPEATS
Precode measures level/risk for the 6 Bredesen subtypes with a reduced panel repeated at 6 and 12 months.

RECODE PANEL AND 6 + 12 MONTH REPEATS
The ReCode panel is the full Bredesen panel with a reduced panel repeated at both 6 and 12 months.

NEUROREADER VOLUMETRIC MRI-BASED REPORT
It may be possible to use existing scan data if a volumetric T1 segment has been run on a brain MRI

COMBINATION OF RECODE AND CIRS/CIRS LITE
This testing combines the work of Dr Bredesen with the work of Dr Shoemaker and assessment of CIRS, measuring additional inflammatory and hormone markers.

BREDESEN PRECODE HORMONE STATUS
Hormone testing can be added to the panels above or run independently.

PRECODE HEAVY METALS PANEL
This panel includes the heavy metals included in the Bredesen Panel, which can be ordered separately or as part of the panel.

Developing a clinical specialism

Example: Neurological Health: A deeper dive into cognitive decline….Antibodies

Alzheimer's LINX™ - Alzheimer's-Associated Immune Reactivity **	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Brain Proteins				
Tau Protein	0.71			0.0-1.2
Amyloid-Beta Peptide	0.77			0.1-1.4
Rabaptin-5 + Presenilin		1.28		0.0-1.4
Alpha-Synuclein			2.27	0.4-1.7
Growth Factors				
Beta Nerve Growth Factor	0.89			0.3-1.5
Brain Derived Neurotrophic Factor	0.77			0.0-1.0
Neurotrophins	0.85			0.5-1.8
Somatotropin	0.70			0.1-1.8
Enteric Nerve, Enzymes and Neurological Peptides				
Enteric Nerve + Vasoactive Intestinal Peptide	0.31			0.0-1.0
Transglutaminases	0.90			0.2-1.3
Pathogens				
Oral Pathogens	0.57			0.2-1.1
Enterococcus faecalis		1.45		0.4-1.8
Escherichia coli CDT + Salmonella CDT	0.46			0.3-1.7
Campylobacter jejuni CDT	0.75			0.0-1.7
Herpes Type-1	0.47			0.2-1.8
Blood Brain Barrier and Neurofilaments				
Blood-Brain Barrier Protein + Claudin-5			2.02	0.2-1.4
Aquaporins		0.82		0.2-1.0
Neurofilament Proteins	0.82			0.4-2.1

Developing a clinical specialism

Example: Neurological Health: A deeper dive continued….. Genetics of cognitive decline

APOE GENOTYPE

ApoE is an apoliprotein important in lipid regulation. Perhaps most well-known for polymorphisms that encode E2,E3,E4. ApoE E4 carriers have a 42% higher risk for CVD and this is highly associated with Alzheimer's.

GENIE TEST

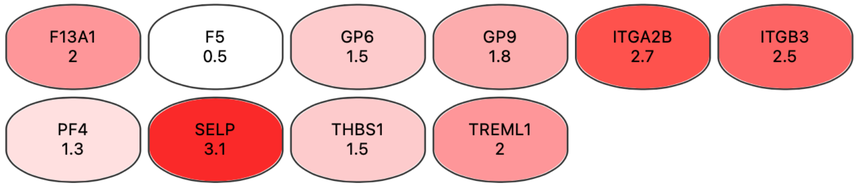
GENIE is a gene expression assay comprised of 188 genes. Establishing how genes are expressing helps us to understand which are over or under-expressing, adding value to the clinical picture and proteomics. The test measures mRNA in white blood cells.

GENETIC CARDIOVASCULAR MARKERS

Test Name	Result	Comments (See Guidance Statements)
APOE GENOTYPE	4/4	Apo E4 Carrier: associated with increased CVD risk.

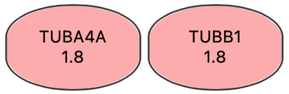
4) Coagulation

Also known as clotting is the process by which blood changes from a liquid to a gel forming a blood clot. It potentially results in hemostasis.



17) Cytoskeleton

Interlinking protein filaments that support cellular structure.



Personalised approach to patient testing

Female patient 30 years old, PhD candidate
Lives in Europe

Key health Concerns:

Cystic Acne and Oily Skin
Missing/irregular periods- concerns surrounding PCOS (dx 2017)/Endometriosis (dx 2014)
Diarrhoea/Constipation- alternating stool presentation
Immune system felt ‘off’ unsure how long that had been going on for
Lives in a high anxiety state that seems at odds with settled life
Muscle weakness and fatigue including frequent sore throat
Low BMI

Had been working with another practitioner who referred them on to me due to environmental concerns

Personalised approach to patient testing

Came to me in December 2022 with:

Borderline urinary mycotoxin test
Elevated Calprotectin
Indications for gut dysbiosis via organic acid testing
T cell testing indicating elevated TH1 and down-regulated TH17

Failed online VCS test and 9/13 symptom clusters indicated on Shoemaker 37 symptom questionnaire

Undertaking a carnivore diet with supervision from previous practitioner to minimise symptoms, which was working in that it was holding certain symptoms at bay but any deviation brought symptoms on, especially GI symptoms

Sister has Coeliac Diagnosis

Health timeline noted changes with home moves & primarily hormones/immune related

Personalised approach to patient testing

In spring 2023 we tested:

GI Map Stool test- H.pylori, Entamoeba coli parasite, low commensal/high opportunistic bacteria, high calprotectin and borderline high zonulin and b.glucuronidase

I**ntestinal Hyper-permeability**- Showed high zonulin, very high LPS, elevated histamine (normal DAO), possible gluten reactivity and possible lactose intolerance

Client was recommended a gut protocol to re-balance flora and eradicate potential pathogens. Update appointment yesterday, moving on to phase II gut protocol to rebalance mucosal lining and all GI symptoms are gone: “like night and day”, anxiety also much reduced

GP had already organised a colonoscopy due to prior calprotectin result- it was negative

Personalised approach to patient testing

Client also concerned about food-immune reactivity- she had come to me with a mugwort borderline positive result, so we tested:

Gluten reactivity- despite being on carnivore approach with no grains for over 8 months wheat germ agglutinin IgA and Glutentin 21 mer IgG/IgA were positive still as well as non-gluten proteins

Gluten-associated cross-reactivity testing- showed clear response to cow's milk, casein & casomorphin, oats, corn, egg and soy as well as all gluten free grains apart from buckwheat & tapioca

General food sensitivity testing showed a high response to many foods indicating high risk for molecular mimicry/epitope spreading

Antibody response testing showed high IgG response to several mould species, CMV, HHV6 & CYP450
Autoimmune testing showed very high phospholipid abs, high platelet glycoprotein and fibulin abs, several neurological antibodies

Personalised approach to patient testing

Client continuing with carnivore approach and being careful to ensure fresh meats/fish are being prioritised to reduce histamine risk

Phase II gut protocol will see some resistant starches being introduced e.g herbs as a first step to expanding the dietary approach

As IgE was also raised we are tracking this with her GP: Could be related to the parasite, could be relating to a food, could be a combination of all of these factors, including the borderline mugwort specific result.

Personalised approach to patient testing

Additional immune/hormone testing showed:

Elevated TGFb1 3060 pg/mL
Leptin low 2.3L
ACLA negative
C4a 14,384 ng/mL
MMP9 1,369 ng/mL
Low aMSH
Gene expression testing showed cellular hypometabolism, B cell activation & indications for environmental trigger for hypometabolic picture
Nasal swab: MARCoNS positive with biofilm

Clear inflammatory process occurring- hits threshold for consideration of environmental trigger so client tested home environment with dust swiffer for mould species and skin swab for actinomycetes
Both came back positive. Client is now undertaking remediation. Client undertaking nasal spray protocol
Client decided to do a fuller hormone test via her Endocrinologist.

Personalised approach to patient testing

Hormone testing showed:

Low progesterone indicators
Low oestrogen/metabolite indicators
Higher androgens with 5a Androstandeiol highest marker
24 hour cortisol was above range with morning and night levels high

Clear indicators that elevated androgens will be driving her skin issues and hormone imbalance.

Endocrinologist considering results in the meantime client is on nutraceuticals to start to work on hormone balance. We have started to have discussions about optimising fertility, and as NK 16+/56+ are positive there is also an immune element involved as well as the imbalanced hormones and underlying endometriosis.

This week we discussed acute changes in her varicose veins and due to DVT risk I have advised she see her Doctor in a timely manner- due previous phospholipid/clot risk results. Could be related to lipid lowering medication she is currently on

Personalised approach to patient testing

The clinical plan is to move on to gut protocol phase II to support mucosal lining and microflora balance. Repeat the stool test during phase II as a straight forward functional repeat.

No further testing relating to hormones while we are assessing protocol for skin. In terms of ranking symptoms client initially said digestive symptoms were the worst, so we focused on that. Now it is the skin as there has not been sufficient change we are focusing on hormones, while still working on underlying gut health.

Regarding fertility as the client is ovulating we are monitoring this at the moment, and will revisit more intensely if we don't see changes in the skin, as this will be reflective of hormone situation. However, if no change in 6-9 months then she will be referred for full fertility assessment.

Regarding immune status. Re-testing will take place in around 6 months so the client will have had a full year on the gut protocol, will have remediated her environment, we will have optimised barrier support and with dietary measures in place too, this will be an ideal time to do a full symptom review. At this point tests will be ordered to track progress for some, and for others they may not be repeated depending on symptom pattern.

https://www.colabeu.com/

- Founded by Louise Carder in 2018- Louise is still a practicing Nutritional Therapist & Venipuncturist
- A UK based test distributor supporting practitioners Europe/Middle East with Colab Services developed panels as well as kits from partner laboratories. Colabs also curate bespoke panels for practitioners. We offer a personalised test service to optimise a personalised healthcare approach; facilitating tests for a functional approach. We offer over 200 tests, organised into 10 body system categories & also specialise in complex logistics e.g. dry ice shipping for specialist markers
- Colab Services also offer specific testing relating to pioneering protocols; including Bredesen panel endorsed by the Apollo Health team, Prodrome Protocol testing endorsed by Prodrome Sciences (both protocols address cognitive decline), CIRS testing endorsed by Dr Shoemaker, Micro-immunotherapy via Lab4more and testing for the Walsh protocol looking at nutrient levels
- Offer blood/bloodspot, nasal swab, saliva, urine/dried urine, stool & breath tests
- Online educational videos and specialist training events, workshops & in March 2024 a Conference entitled ‘Does Mould Matter? And our annual Biotoxins in Clinical Practice Course’
- Technical support team to support with test questions & test results
- Excellent customer service team, dedicated to supporting our registered practitioners

Thank you

For further contact/queries: louise.carder@colabeu.com
Website: www.colabeu.com

Events: www.colabeu.com/events
Biotoxins in Clinical Practice Course:
January - March 24 (3x 2 hr online sessions with a live day in London 8.3.24)

March 7th 2024
Biotoxins Masterclass- intensive workshop (PM session- live in London)
Meeting of Mould Minds- global round table updates (evening session- online)

March 9th 2024
Does Mould Matter? Conference (Live- London 9am-5pm)