

A Microbial State of Mind: Inside the Gut-Brain Axis

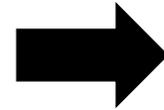
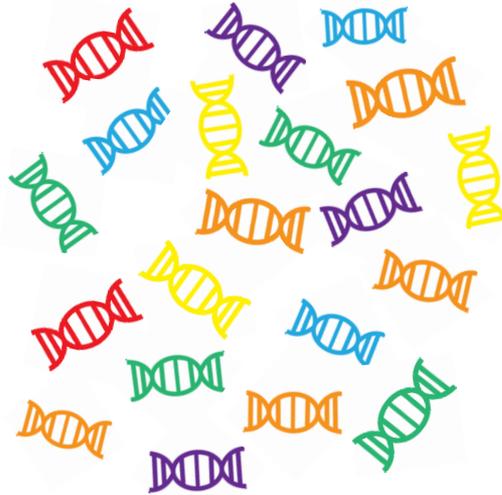
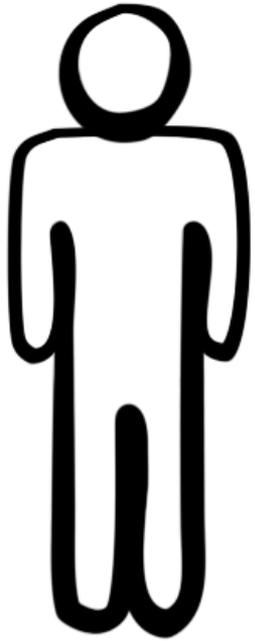
Jonathan Swann

Professor of Biomolecular Medicine
Director of the UK Gut-Immune-Brain Axis Network+
School of Human Development and Health
Faculty of Medicine,
University of Southampton



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Collectively known as the **Metagenome**



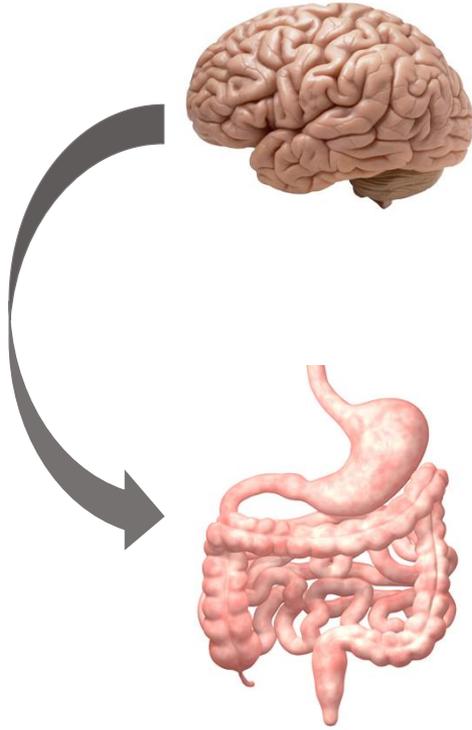
100X

more genes than
human genome

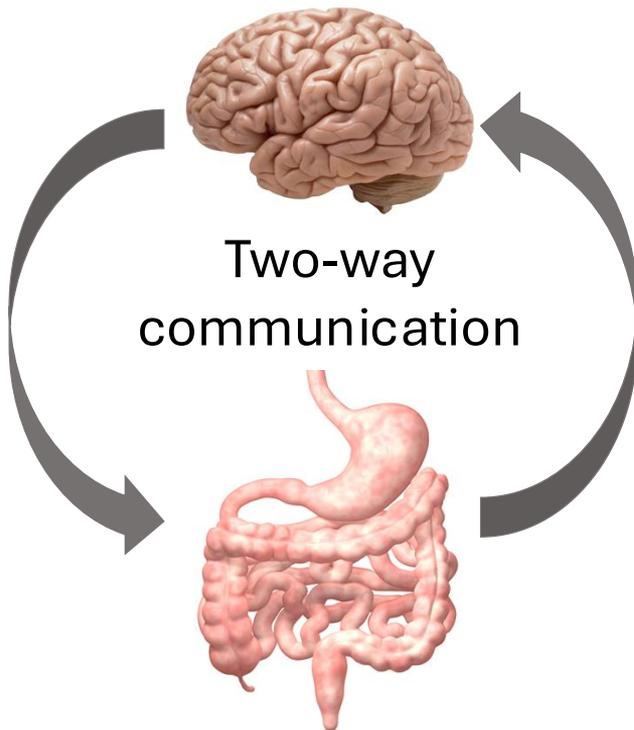
= biochemical functions

- **Metagenome** contains more than **3 million microbial genes**
- **Human genome** contains ~24,000 genes

Gut-Brain Axis



Gut-Brain Axis



guts

Courage. synonym:
Intestinal Fortitude

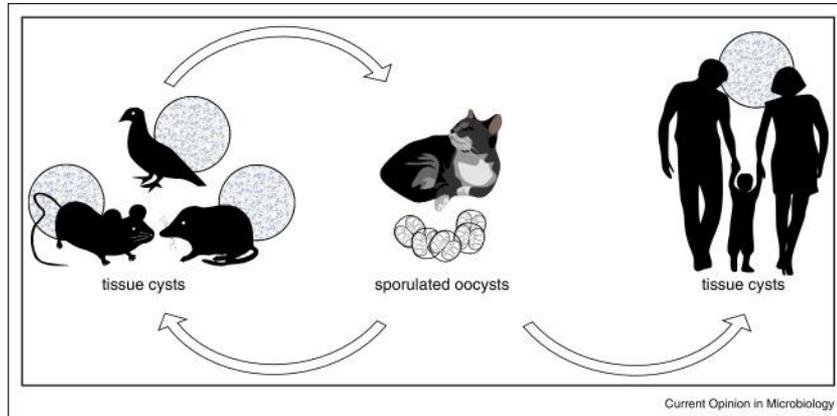
you don't have the guts
for that

ud



Toxoplasma gondii

- single celled pathogen
- Toxoplasmosis



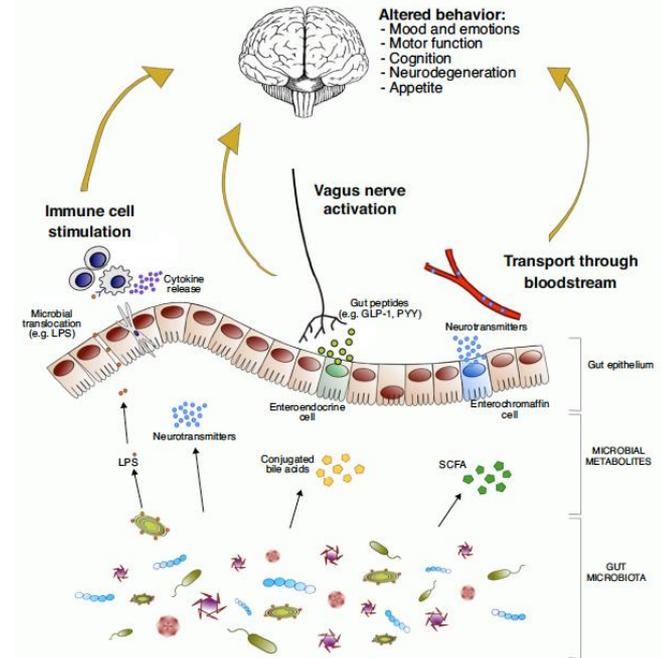
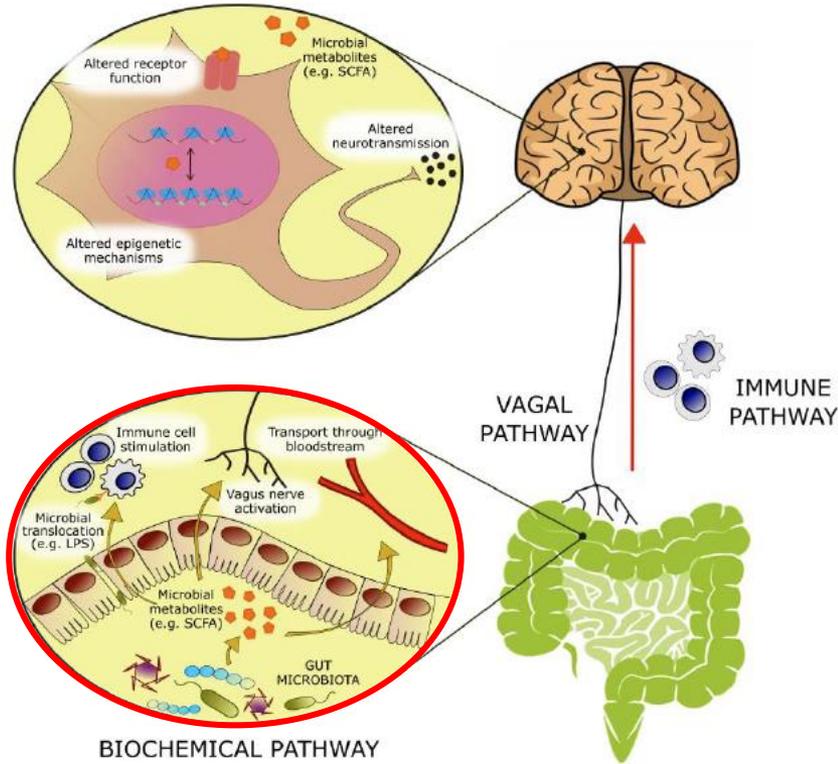
Horsehair worm

Nematomorpha



Image from: The Wildlife Trusts

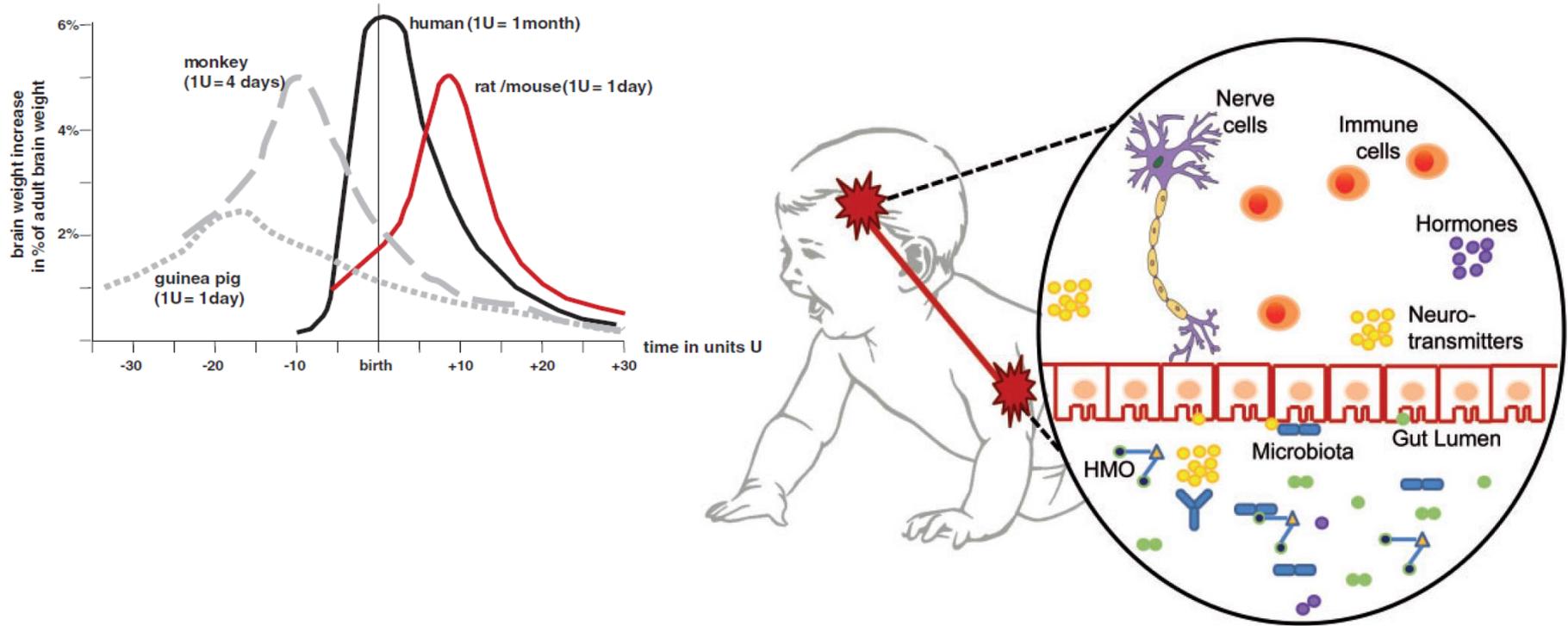
Microbiota-Gut-Brain Axis



Caspani et al. (2019) *Microbial Cell* 6(10)

Caspani & Swann (2019) *Curr Opin Pharmacol* 48.

Most (>75%) of Human Brain Growth & Development Occurs in the First 2 Years of Life



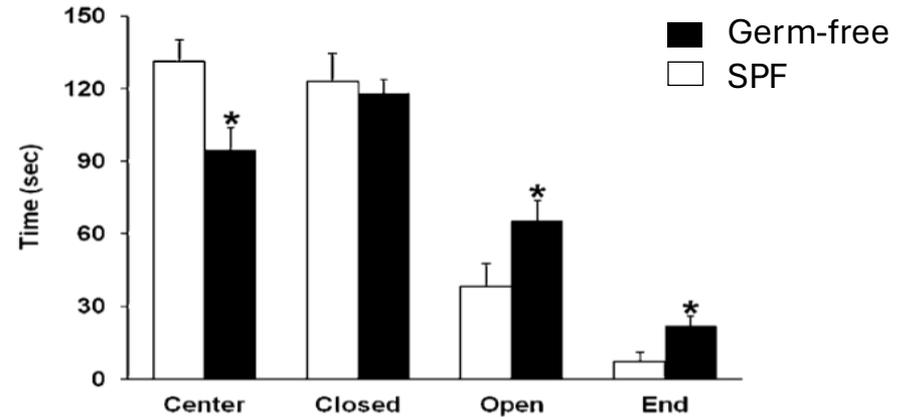
Normal gut microbiota modulates brain development and behavior

Rochellys Diaz Heijtz^{a,b,1}, Shugui Wang^c, Farhana Anuar^d, Yu Qian^{a,b}, Britta Björkholm^d, Annika Samuelsson^d, Martin L. Hibberd^c, Hans Forsberg^{b,e}, and Sven Pettersson^{c,d,1}

PNAS | February 15, 2011 | vol. 108 | no. 7 | 3047–3052

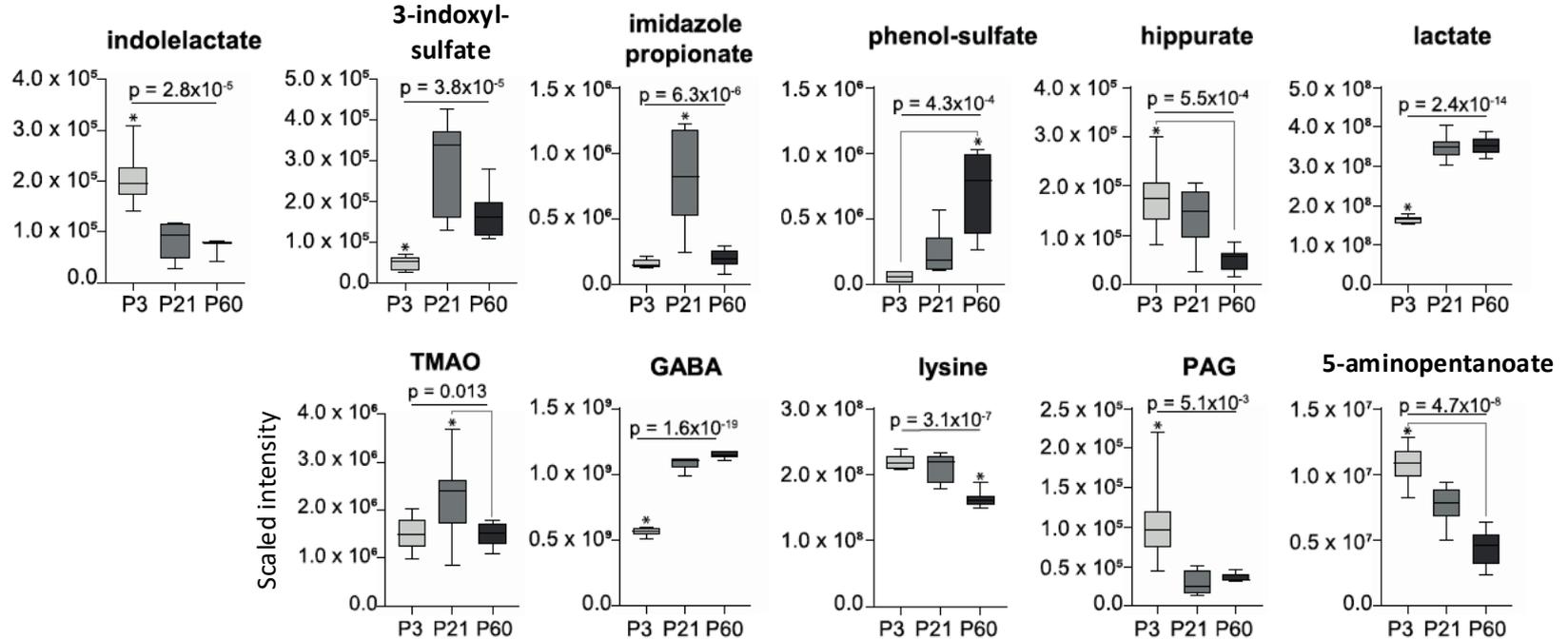


GF have reduced anxiety-like behaviour



Perinatal period critical for this developmental programming – changes not reversed if mice colonised after 6 weeks

Gut microbial-related metabolites in the forebrain



The maternal microbiome modulates fetal neurodevelopment in mice

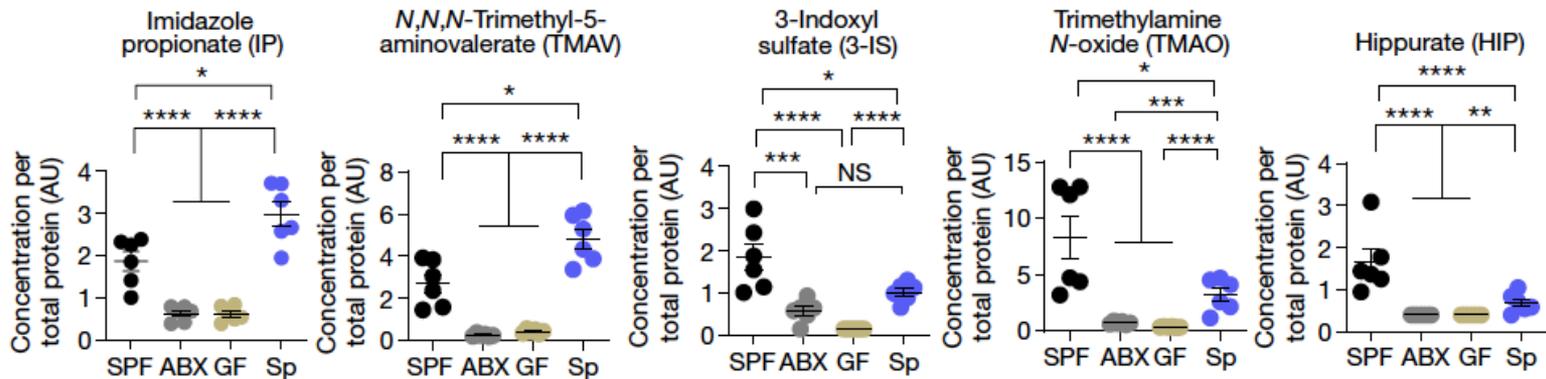
Nature | Vol 586 | 8 October 2020 | **281**

<https://doi.org/10.1038/s41586-020-2745-3>

Helen E. Vuong^{1,2}, Geoffrey N. Pronovost¹, Drake W. Williams², Elena J. L. Coley¹, Emily L. Siegler¹, Austin Qiu¹, Maria Kazantsev¹, Chantel J. Wilson¹, Tomiko Rendon¹ & Elaine Y. Hsiao¹

Received: 23 July 2019

Accepted: 24 August 2020

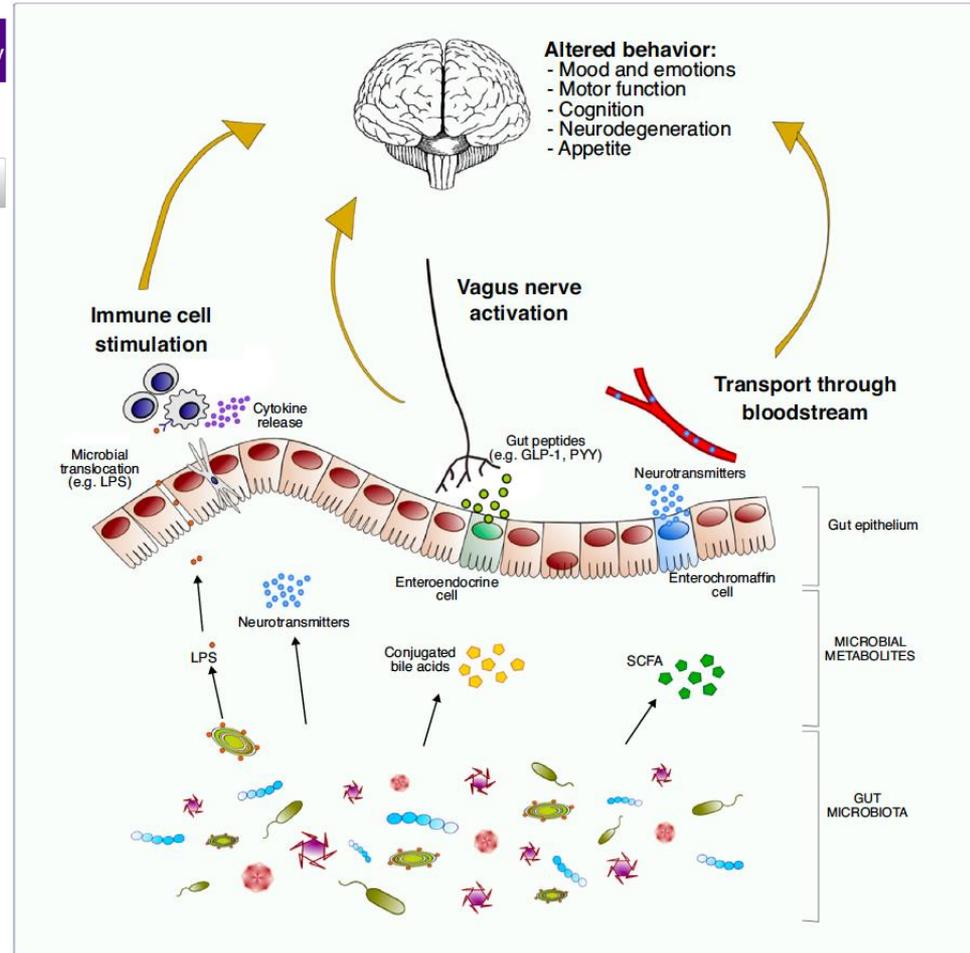


Small talk: microbial metabolites involved in the signaling from microbiota to brain

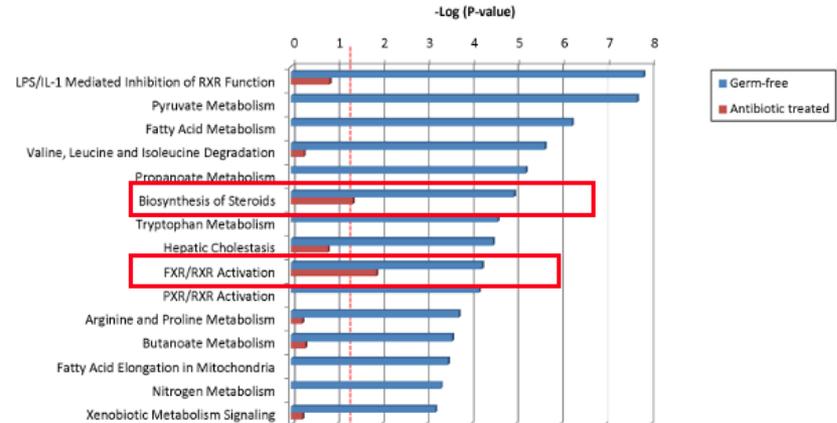
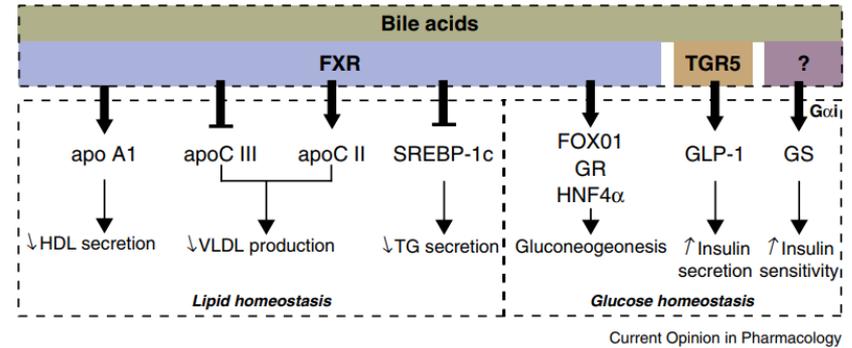
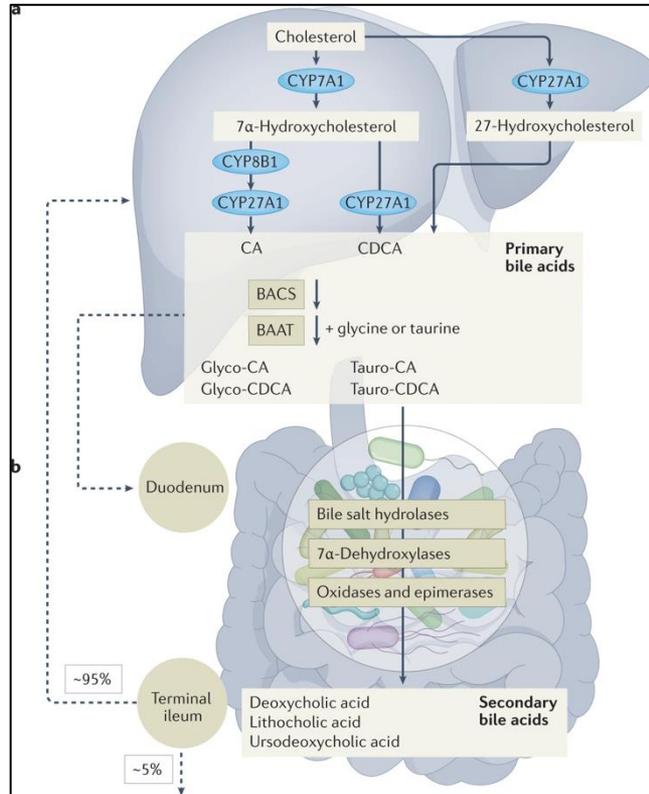
Giorgia Caspani and Jonathan Swann



- Neurotransmitters
- Bile acids
- Short chain fatty acids (SCFA)
- Indoles & tryptophan
- Cresols
- Lipopolysaccharides (LPS)
- Lactate
- Choline
- Vitamins

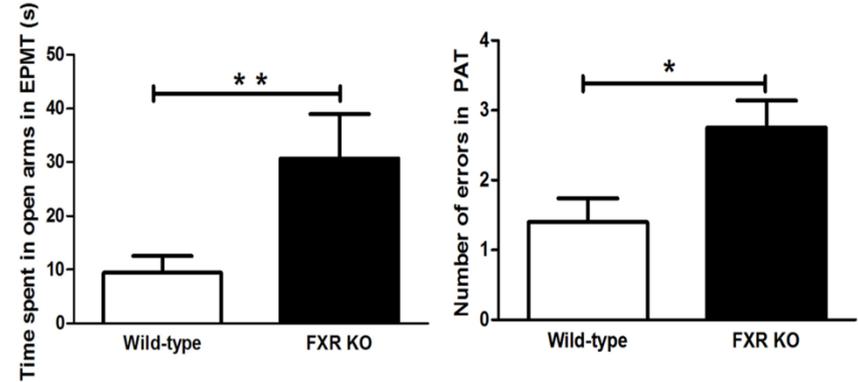


Bile acids: trans-genomic signaling molecules



Deletion of mouse FXR gene disturbs multiple neurotransmitter systems and alters neurobehavior

Fei Huang¹, Tingting Wang¹, Yunyi Lan¹, Li Yang¹, Weihong Pan², Yonghui Zhu¹, Boyang Lv¹, Yuting Wei¹, Hailian Shi¹, Hui Wu¹, Beibei Zhang¹, Jie Wang¹, Xiaofeng Duan³, Zhibi Hu^{1*} and Xiaojun Wu^{1*}

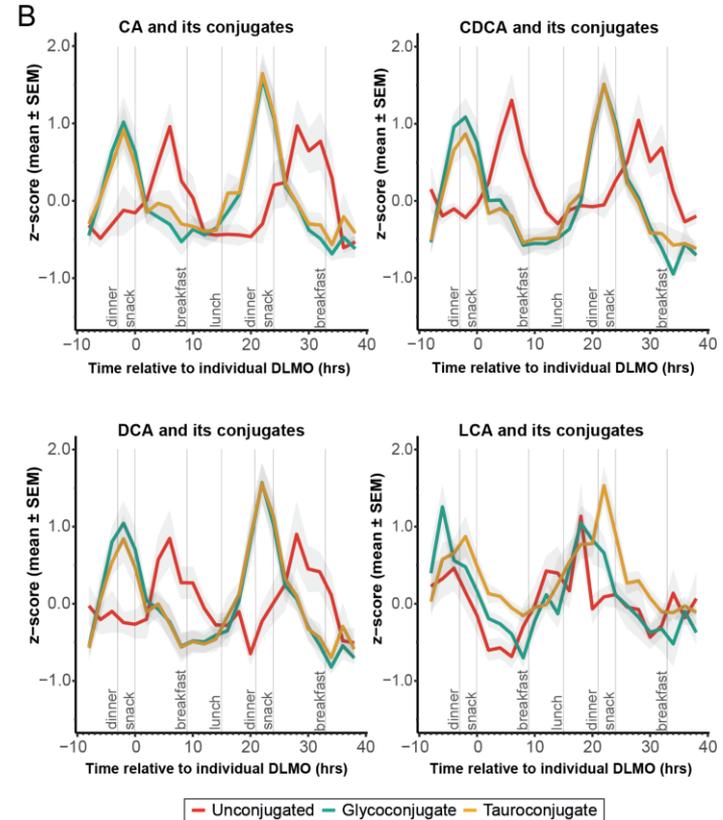
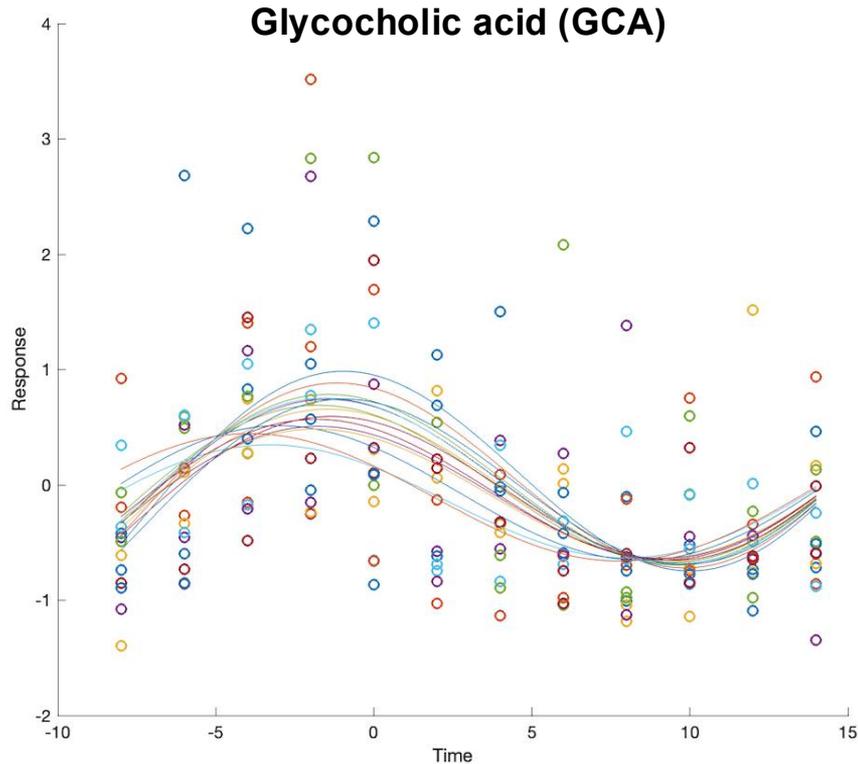


Neurotransmitters	Hippocampus		Cerebellum		Prefrontal cortex	
	Wild-type	FXR KO	Wild-type	FXR KO	Wild-type	FXR KO
GABA ($\mu\text{g/g}$)	168.845 \pm 21.772	171.059 \pm 31.045	16.452 \pm 0.680	20.717 \pm 0.444***	53.232 \pm 7.960	51.664 \pm 4.475
Glu ($\mu\text{g/g}$)	195.757 \pm 27.440	156.079 \pm 29.175	7.456 \pm 0.530	7.821 \pm 0.421	56.118 \pm 9.310	50.784 \pm 6.171
DA (ng/g)	47.757 \pm 3.438	45.840 \pm 4.431	N.D.	N.D.	N.D.	N.D.
NE (ng/g)	2216.645 \pm 304.033	1791.320 \pm 169.453	1542.997 \pm 140.334	1911.069 \pm 25.808*	8935.464 \pm 876.937	7894.620 \pm 912.644
Epi (ng/g)	33.290 \pm 2.606	32.543 \pm 2.992	N.D.	N.D.	N.D.	N.D.
5-HT (ng/g)	54.272 \pm 7.440	55.936 \pm 4.716	18.580 \pm 3.684	21.735 \pm 0.960	319.803 \pm 34.737	310.598 \pm 41.824
5-HIAA (ng/g)	532.423 \pm 45.891	561.231 \pm 51.504	165.938 \pm 20.185	240.796 \pm 7.137**	1158.452 \pm 145.803	1269.219 \pm 126.655
GABA/Glu	0.897 \pm 0.057	1.149 \pm 0.066**	2.135 \pm 0.119	2.761 \pm 0.132**	0.993 \pm 0.056	1.062 \pm 0.065
5-HIAA/5-HT	10.638 \pm 0.763	10.310 \pm 0.654	9.316 \pm 0.800	11.329 \pm 0.760	3.822 \pm 0.460	4.477 \pm 0.499

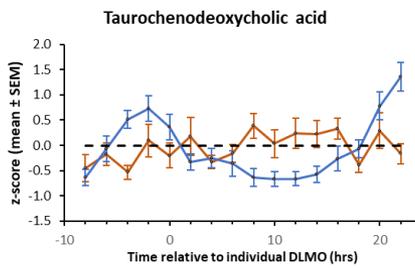
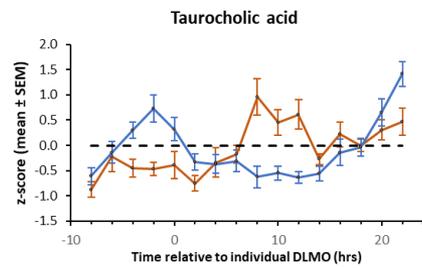
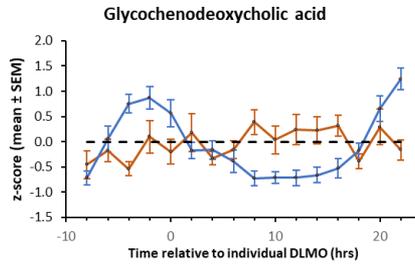
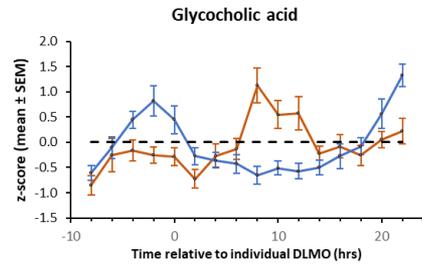
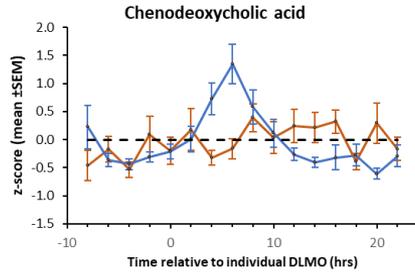
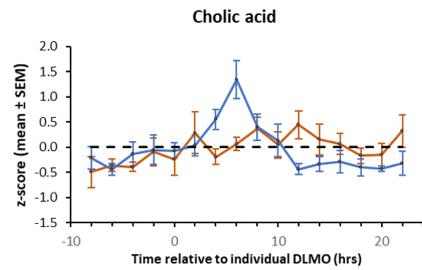
FXR KO mice

- Less depressive-like behaviour
- Less anxiety-like behaviour
- **Impaired memory**
- Reduced motor coordination
- Changes in neurotransmission

Plasma bile acids have a daily rhythm



Plasma bile acids are regulated by environmental cues



— Entrained study (CRC286) — Constant routine (CRC307)



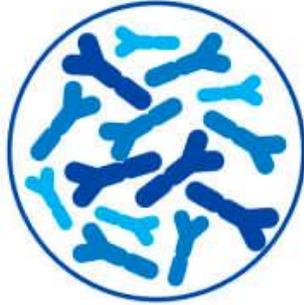
Implications for shift workers & jetlag

Effects of Factors Related to Shift Work on Depression and Anxiety in Nurses

Yuxin Li^{1†}, Yongchao Wang^{2,3†}, Xiaoyan Lv^{4,5}, Rong Li^{4,5}, Xiangyun Guan^{4,5}, Li Li^{4,5}, Junli Li^{4,5} and Yingjuan Cao^{1,4,5*}

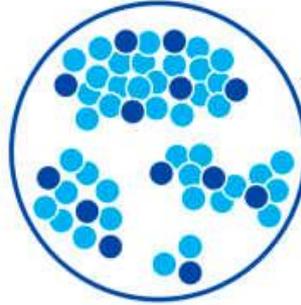
Frontiers in Public Health (2022)

- Shift nurses:** 62.08% depression; 58.82% anxiety;
- 1.54 and 1.36 more likely than non shift workers



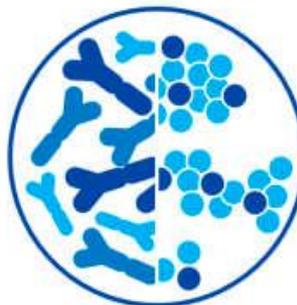
Probiotics

Live microorganisms that confer a health benefit on the host when administered in adequate amounts



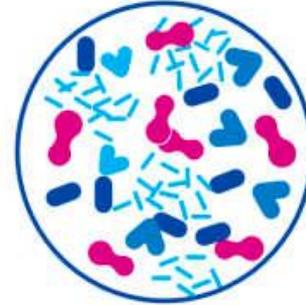
Prebiotics

Substrates that are selectively utilized by host microorganisms conferring a health benefit



Synbiotics

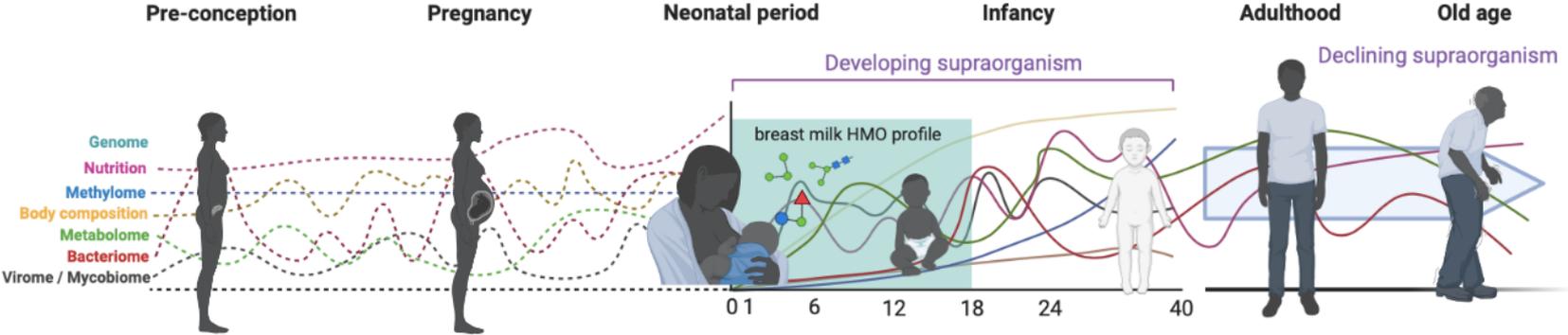
Combination of both probiotics and prebiotics



Postbiotics

Compounds produced by microorganisms, released from food components or microbial constituents, including non-viable cells that, when administered in adequate amounts, promote health and well-being

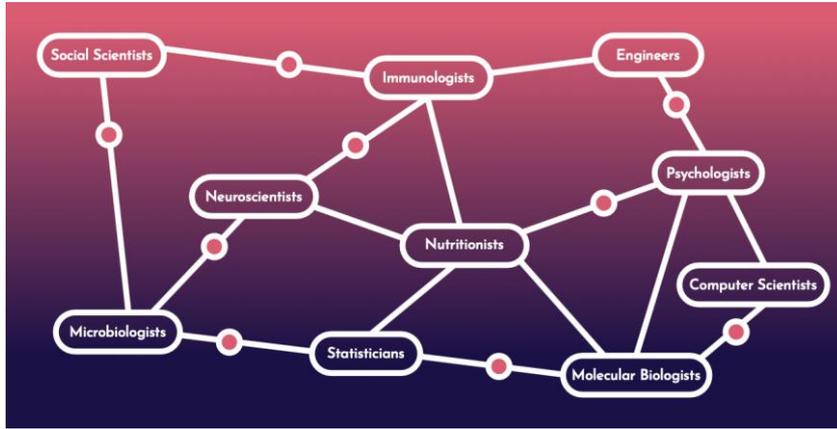
Supraorganism across the lifecycle





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Fellowships: £500,000

Deadline: 15th April



Acknowledgements

j.swann@soton.ac.uk



**UK GIBA
NETWORK+**

University of Southampton

- Dakshat Trivedi
- Lizzie Wimborne
- Veronica Santiago
- Michael Harvey
- Savannah Rivera
- Kate Pearse
- Dan McCann
- Madhuri Panchal

Karolinska Institute

- Rochellys Diaz Heijtz

Imperial College London

- Elaine Holmes
- Adesola Bello
- Natasa Giallourou
- Sonia Spitzer
- Marine Letertre
- Giorgia Caspani
- Ian Wilson

University of Oxford

- Phil Burnet

IDIBGI

- Jordi Mayneris-Perxachs
- Jose-Manuel Real-Fernandes

University of Surrey

- Debra Skene
- Daan Van der Veen

University of North Carolina

- Matthew Redinbo
- Aadra Bhatt



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NUTRITIONAL CARE IN INCURABLE CANCER

Amy McLuskie

HCPC Registered Dietitian

Clinical Research Fellow

PhD Candidate

University of Edinburgh





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BACKGROUND

Malnutrition

- Prevalent in adults with cancer.
 - 40% to 60%, depending on the type of cancer and stage.
- Underlying disease, treatment and/or the effect of nutrition impact symptoms.
- Higher risk of treatment-related side effects, delays in treatment, increased hospital admissions, decreased quality of life, and survival outcomes.
- An estimated 10-20 % of patients die due to malnutrition rather than the tumour itself.
- Under recognised and undertreated in clinical practice
- 36% of people in UK with cancer who require nutritional intervention are referred to a dietician.



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QUALITATIVE STUDY: INVESTIGATING PEOPLE'S PERCEPTION AND EXPERIENCES OF NUTRITIONAL CARE IN ONCOLOGY (IPEN).



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Aim:

To explore the meaning that people with incurable cancer and their caregivers attach to weight loss, nutrition and nutritional care.



Source: Photo by Kzenon on Canva



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METHODOLOGY

- Interpretative Phenomenological Analysis (IPA)
- Data collection through semi-structured interviews and field notes
- Purposive sample
- Study opened April 2025
 - 18 participants in total contacted
 - 12 participants recruited
- All interviews except one were conducted in the home setting
- Interviews ranged from 12-80 minutes (mean duration 43 minutes)
- Information power reached at interview 10



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PARTICIPANT DEMOGRAPHICS

Participant	Gender	Age	Cancer Diagnosis	Ethnicity	Involved as	Support received from a dietitian
P1	F	71	Non-small cell lung	A	Person with cancer	No
C2	M	80	N/A	A	Supporting role (husband)	No
P3	F	69	Non-small cell lung	A	Person with cancer	No
C4	M	77	N/A	A	Supporting role (husband)	No
P5	M	74	Metastatic pancreatic	A	Person with cancer	No
P6	F	75	Pancreatic	A	Person with cancer	No
P7	M	66	Primary liver	A	Person with cancer	Initial telephone call
C8	F	35	N/A	A	Supporting role (daughter)	No
P9	F	54	Gallbladder	A	Person with cancer	Yes
C10	M	57	N/A	A	Supporting role (husband)	Yes
C11	F	63	N/A	A	Supporting role (sister)	N/A
P12	F	77	Cholangiocarcinoma and secondary bowel cancer	A	Patient	No

A: White: English/Welsh/Scottish/Northern British/British



THEMES AND SUBTHEMES

Nutrition and nutritional care experiences in those with incurable cancer and their caregivers

1. 'The disappearing body'

1. Making sense of the weight loss
2. A lifelong relationship with weight and a sense of control

2. Anxiety and negative emotions

1. Anxiety that never leaves
2. A sense of loss around weight and eating
3. Conflict, pressure, and guilt
4. The emotional toll of caring and feeling unheard

3. Coping and adapting

1. Adapting and finding new ways to deal with the changes
2. Acceptance of illness

4. Food and social connections

1. Food as pleasure and social connection
2. Eating for one with incurable cancer

5. 'Just winging it': Experiences of advice and support

1. The problem with generic advice
2. Managing this ourselves and hoping for the best
3. Lack of support available
4. Benefits of professional input

PARTICIPANT QUOTES: THEME 1

- **The disappearing body**

- **Making sense of the weight loss**

Just the same as normal, I've always ate and drunk (pause) so its no [not] been a problem just this disappearing weight where's it gone I don't know. P 1

'cause I'm looking at him going, I think you have cancer, I think you have cancer.But then, I just knew, I knew he had cancer from that point, because I could see how thin he was. And then, we went down for dinner on the Saturday night, and came out the lift, and again, got the shock of my life. I was completely taken aback at the weight loss.' C 8

- **The relationship with weight**

And then at one point I thought, oh this is great, because I've been waiting to lose weight for years. But, erm, obviously it was coming off very quick, it was only a couple of months, and I lost, I think, about three, three and a half stone, so it was quite drastic. P 9



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PARTICIPANT QUOTES: THEME 3

Coping and adapting

- Adapting, finding new ways to deal with the changes

So, aye, it's, er, you're eating less, that's, that's the one thing, because you're tired, you're not exercising, you've got muscle loss, you're not as strong as you used to be. I can still do everything, still get dressed, and showered, and all that kind of stuff. It's a struggle, it's a struggle, but it's new, everything's brand new to you. P 7

The eating and drinking is hard. I've stopped drinking coffee, I'm sticking to water most of the time, I'm drinking a lot more water. Eating smaller meals, plainer meals, as I said. [Pause]. And just eating when I feel like it, rather than, it six o'clock, news time, dinnertime. Just, yeah, erm [pause], it's more of a chore, rather than a fun thing, yeah.' P 12



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PARTICIPANT QUOTES: THEME 4

Food and social connections

*But you cannae sit here and be a recluse and say to yourself, no, that's not for me.....On Monday, and we went for some tapas at the, er, [place]. We had it all planned, and as I said to you, I took some fancy dishes, three fancy dishes, and I cleared the plate.....Erm, it was interesting to watch, that the conversation on Monday was non-stop, four hours. I had a couple of drinks as well when I was there, I thought, there's got to be a part of you that says, you've got to stay real.....So anyway, but no, the conversation with the food, the conversation made, makes you more relaxed, easy. **P 7.***

*A wee bit cut off, maybe. And I know the longer it happens, the more and more I'm gonna come off, cut off from people. So then, how do you reclaim that? I don't know. I have to face that when it comes [laugh]....Well, like tomorrow, I should be going down to meet a group of old friends, all of a same age, for bacon rolls and coffee at the [place], and I can't. I can think of nothing worse at the moment than sitting in the [place] having a cup of coffee and a bacon roll. **P 12***





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PARTICIPANT QUOTES: THEME 5

'Just winging it', Experiences of advice and support

I just kept thinking, how, how can I get through this, how can we get through this. And it got to the point where I did order the drinks off Amazon, 'cause I thought, I'm gonna, if no one else is doing something, I'm gonna have to....And I just had to wing it, genuinely, just had to wing it. C 8

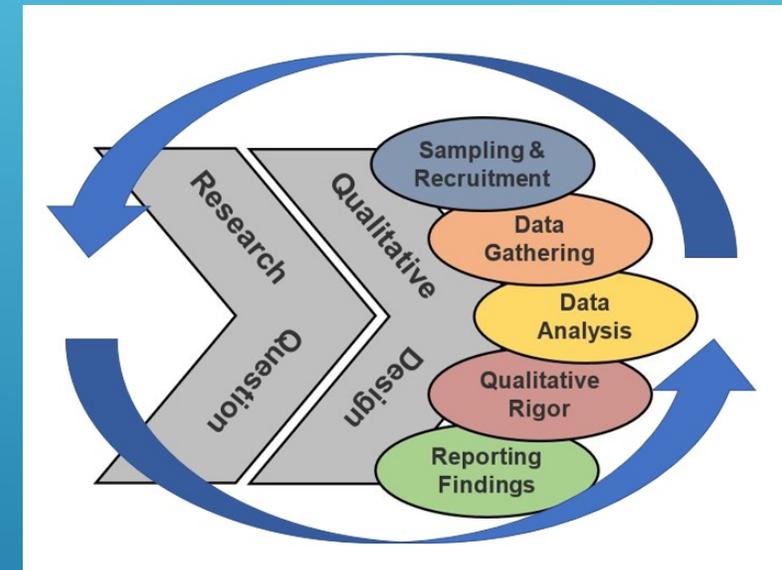
Well they, they immediately said to me that they would get a dietitian on board, fair enough, that's cool. I got a letter through the door saying, well you've been registered with us, we'll be in touch within fourteen to sixteen weeks. And I thought, well if that's what it is, that's what it is, these guys are in demand. P 7

well I think it would be a dietitian had been part of the process and that so basically the...part of the course, you've seen the consultant and been referred to the treatment, we were told that the nurses are available to you if there's something wrong, but no speaking to a dietitian to speak you through what the possibilities are in the future and that. C 4

Erm, so yeah, it's definitely, erm, it's been a learning curve, definitely, erm, and it's been manageable because it's been explained well, and it's been well thought about, you know, what you have to do in order to manage it. And you could still get on with your life, so it doesn't have to take over your life, erm, it's just part of my life now. Erm, so it's good, because I'm not having to stop going out socialising, and meeting with my friends, and things, and going for lunch. P 9

FINDINGS

- Eating and weight loss are far more than merely nutritional concerns.
- Emotive aspects of accepting bodily change.
- Importance of strong social connections.
 - Changes in the ability to eat and drink → social isolation
- Caregivers felt compelled to 'wing it' due to inadequate nutritional care
 - Caregivers to be involved in education, anticipatory conversations and emotional support
- Nutritional needs, both physical and psychological, are unmet due to a lack of nutritional care
- Greater emphasis on weight, rather than on quality of life





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CLINICAL IMPLICATIONS

- Nutritional care for people with incurable cancer who are at nutritional risk should be prioritised, timely and responsive to evolving individual needs (13-15).
- Healthcare professionals should engage in open, anticipatory conversations about expected changes in appetite, intake, and weight
- Essential to look for signs of social withdrawal and caregiver burnout, and to escalate this
- Caregivers need to be more explicitly involved in nutritional care
- Healthcare professionals should also acknowledge the emotional significance of food and encourage and support social eating
- Dietitians should be integrated into oncology and palliative care teams and cancer pathways

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THANK YOU

ANY QUESTIONS?

