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Innopharma Insights

Volume 2

Contents

Editor's Introduction

As Editor-in-Chief, it is my pleasure to welcome you to the second volume of Innopharma Insights. This milestone marks a significant continuation and affirmation of our commitment to fostering and showcasing the exceptional research, innovation and expertise within the Innopharma Education community.

Building on the strong foundation laid by our inaugural issue, this volume reflects our vision to serve as a dynamic platform bridging academia and industry in the pharmaceutical, medical device and food science sectors. It signals our dedication to ongoing knowledge exchange, collaboration and insight generation that addresses both current challenges and emerging trends within the life sciences.

Volume 2 delivers a wide variety of content featuring practical career guidance for graduates entering biopharmaceutical manufacturing, insights on research at Innopharma Education, innovative food product developments and critical discussions on compliance in digital health technologies for diabetes care. Alongside these themes, the volume also touches on sustainable and environmentally conscious approaches, including aspects of green chemistry, reflecting the broader commitment to responsible innovation. The issue also includes diverse research articles derived from original master's dissertations covering advanced therapeutic optimisation, digitalisation of clinical assessments, global usability of medical imaging technologies and psychobiotic nutritional strategies for mental health.

We invite all our readers — learners, academic staff, industry professionals and researchers — to actively engage with the insights shared, contribute their own expertise and help shape the future editions of Innopharma Insights. This journal aims to foster collaboration, support innovation, and facilitate professional development within our community.

My sincere thanks go to the contributors and the editorial team whose dedication ensures the highest standards of quality and relevance. As we celebrate this second issue, we also look ahead with enthusiasm to strengthening engagement, extending our reach and evolving alongside developments in science, technology and education.

Happy reading!

Editor-in-Chief | Colm O'Connor

College Librarian & Research Specialist

Innopharma Insights Editorial Team

Insights| Navigating the Biopharmaceutical Manufacturing Industry Job Application Process: A Practical Guide for Science and Engineering Graduates

Author: Luke Kiernan

Luke is the Managing Director of Technical Services at Innopharma. He has over 25 years of experience within the pharmaceutical industry and lectures across several programmes.

Here, giving his insights to our readers, Luke offers a practical guide for graduates aiming to secure jobs in the competitive biopharmaceutical manufacturing industry in Ireland. He addresses key challenges such as gaining initial experience and provides detailed advice on tailoring CVs to job specifications, effective interview techniques and follow-up strategies.

Breaking into Ireland's biopharmaceutical industry offers rewarding and lucrative career opportunities. However, competition is fierce, requiring strategic planning and a tailored job application approach. This article outlines crucial steps: tailoring your CV, excelling in interviews and effective follow-up to help you stand out.

Understanding the Biopharmaceutical Industry Landscape

Ireland is a leading location for multinational biopharmaceutical investment due to its pro-business environment, skilled workforce and EU access. Industry employers not only look for technical expertise, they also value candidates who demonstrate attention to detail, a quality mindset, a systems-driven approach to work, good communication skills and are a team player comfortable collaborating in cross-functional teams.

Before diving into the application process, it's crucial to understand the varied roles open to science and engineering graduates. Scientists and engineers are highly sought after in roles across manufacturing, quality control, quality assurance, regulatory affairs, validation, operational, projects, engineering and maintenance. While identifying the area that aligns with your skills and interests is important for job

satisfaction, the immediate biggest challenge for new graduates is securing any entry-level role. It is often more effective to view your desired specialism as the career destination rather than the starting point. Once in, opportunities open for movement and experience is easily transferable across companies. All biopharma firms operate under the same HPRA regulations and licensing, ensuring skills remain relevant across the industry.

Research and Identify Opportunities

You should research companies' websites, industry-specific websites, and professional networks like LinkedIn and set up alerts for openings.

Biopharmaceutical manufacturing plants are situated across Ireland and since these plants are spread throughout the country, consider how flexible you can be when it comes to relocation for your first role. Remember, this is just the beginning of your career journey - once you gain experience, your skills will become transferable, making future career moves much easier.

Adapt Your CV to the Job Specification

One common mistake is using a 'one-size-fits-all' CV. In the pharmaceutical industry, this rarely works because companies get hundreds of applications per role. CV review is given less than 30 seconds on average, so tailoring them to the specific job is essential. Another mistake graduates make is assuming they have no experience. Part-time jobs, summer work, college placements or overseas work experience all count as experience. These experiences show valuable life skills like resilience, teamwork, and responsibility. Leaving them off is a missed opportunity. You may be questioned in an interview on any line item in your CV and need to have the facts when answering. Do not be economical with the truth.

CV Tips for success

- ***Tailor Your CV for Each Role***
  Carefully read the job description and highlight key skills, qualifications and experience. Use these keywords directly in your CV—if "teamwork" is emphasised, include it.

- ***Structure and Clarity***
  Ensure your CV is clear and concise, structured with key sections such as Professional Profile, Skills/Competencies, Work Experience and Education.

- ***Professional Profile***
  Use 3–4 sentences to highlight experience, expertise and career goals relevant to the role. This section is critical as it may be the first, or only, part that hiring managers read.

- ***Skills/Competencies***
  Highlight 9 competencies based on the job spec. List the most important first and be ready to discuss examples in an interview.

- ***Work Experience***
  Use bullet points with clear action verbs (e.g., managed a team, generated reports). Include soft skills (communication, teamwork) in your descriptions. Usually 5–6 bullet points suffice; for shorter roles 1–2 points are fine.

- ***Education***
  List course, college, and years attended without unnecessary location details if the college is well-known (e.g., DCU, UCC). Include your final year project title if relevant, as it can be a good interview topic.

The Interview Process

Once you have been called for an interview, it is essential to prepare properly. Research the company to understand their mission, vision and values, their product portfolio, any recent news (expansion, new products, etc). The company website is a very valuable source of information.

Interviews in the pharmaceutical sector tend to be structured. The interviewer may explore your technical expertise but for recent graduates the interviewer is more interested in your broader behavioural fit. Inevitably, nearly every interview begins with the open-ended question: "*Tell me about yourself*" or "*Talk me through your CV*".

This question is simple but is asked to get the interviewee speaking which will help you to relax into the interview. The main purpose of the interview is to understand your personality and assess whether you fit well within the pharmaceutical industry and the existing team. From your CV, the interviewer will understand your technical capability based on your qualifications and any manufacturing experience you may have.

Your "*Tell me about yourself*" is your chance to show motivation, values and thought process. Avoid providing a full chronological life story. Instead, focus on important

aspects like why you chose your course, what you enjoyed (e.g., passion for science, practical work) and what you learned from summer jobs (e.g. teamwork, problem-solving and responsibilities like opening or stocking shelves using a FIFO approach). Prepare examples and keep this answer around 3 minutes, ideally under 5. If you find it is over 5 minutes you need to reduce the content; never speak faster to get it all in. Quality over quantity is the essence of your "*tell me about yourself*".

During the interview, connect with the interviewer by being yourself and letting your personality show. Too much seriousness can create barriers. A simple smile when introduced can break the ice, foster trust and make it easier to connect.

It is important to show energy and enthusiasm for the role. Nervousness is common, and to a degree is expected, but preparation helps. Preparation is the key, and better prepared candidates tend to become less nervous as the interview progresses – the interview will become more like a conversation. Practice your '*Tell me about yourself*' by using AI interview prep tools or recording it and reviewing for clarity, engagement and articulation of your competencies.

Ask yourself: *Would you hire you*?

Lastly, ensure you listen to the question fully and answer the question that is being asked. Many interviewees do not actively listen to the whole question. They hear one word and proceed to speak about that subject and miss the point.

After the Interview

Reaching out to thank the interviewer: It is good to send a thank-you email within 24 hours, expressing how nice it was to meet the interviewer, appreciation for the opportunity, reiterating your interest in the role and briefly highlighting how your skills align with their needs.

Interview Outcomes

The two possible outcomes from the interview process are that you are either successful or unsuccessful. If successful, well done, you are now at the beginning of your journey, and the world is your oyster.

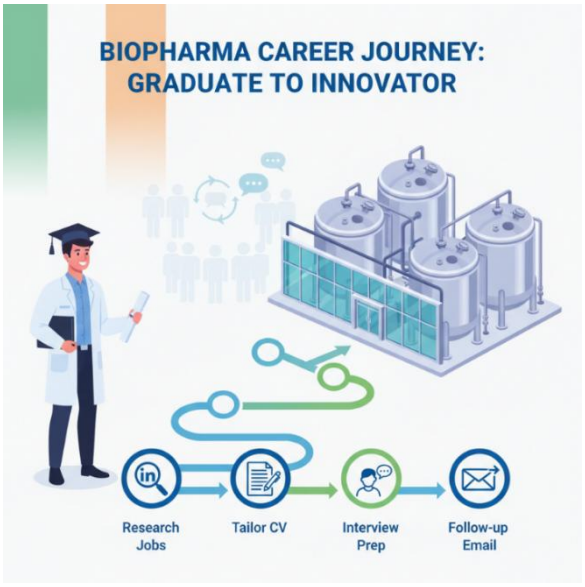
If you are unsuccessful, it is not the end of the world. You may have felt that you did not perform at your best in the interview. If that is the case, then you will learn from the experience and be better the next time. Alternatively, you may have felt that you performed well at the interview. However, you do not know who else was interviewing

for the role. You may have lost out to a more experienced candidate; you may have been down to the last two candidates – the truth is that you don't know how close you were to being offered the role. What is really important is to respond to the interviewer, thanking them for the opportunity, asking for any feedback on how you performed at the interview, advice on how you can improve for future interviews and letting them know that if another opportunity comes up in their organisation that you would love to be considered again. This shows maturity, proactiveness and ongoing desire to work with the company. If the chosen candidate withdraws or accepts another offer, you could be next in line.

Final Thoughts

Breaking into the pharmaceutical industry requires time, patience and perseverance. Rejections and setbacks are all part of the journey—but they do not define your worth or your future. Every application you send, every interview you attend and every connection you make represents progress. Stay focused on your long-term goals and don't be discouraged by short-term obstacles. The right opportunity often comes when you least expect it—but only if you keep moving forward. Believe in your potential, trust your journey and never give up. Your persistence will pay off.

Good luck!



Insights | Finbarr Sheehy

Interview | Questions by Jennifer Manning

Finbarr Sheehy is the Director of Post Graduate Programmes and Research at Innopharma Education. With over 30 years of senior-level experience across the semiconductor, pharmaceutical and digital sectors, Finbarr has played a pivotal role in shaping Innopharma Education's research culture and academic direction. Jennifer Manning holds a PhD in Physiology from UCC, lectures for Innopharma Education and is the Head of Academic Programmes.

In this conversation, Finbarr reflects on the evolution of research within the faculty, the importance of critical thinking in education and how Innopharma continues to innovate through digital transformation, sustainability and close collaboration with industry.

Q: *Tell us about the evolution of research in Innopharma Education.*

At Innopharma Education, research has become a big part of who we are. What started out as practical, industry-focused projects has grown into a culture of curiosity, questioning and real purpose. Today, we don't just ask *how* things work — we ask *why* they exist and *how* they can be made better for people, systems and society. Our learners are encouraged to challenge ideas, test new approaches and think across boundaries — where science, technology and ethics meet.

For us, research isn't about quick answers. It's about having the courage to question, the discipline to dig deeper and the insight to make a real difference. We've moved from simply gathering information to creating knowledge — and ultimately, to finding wisdom through reflection.

Q: *Can you explain the importance of research in undergraduate and postgraduate programmes, particularly in the areas of digital transformation and process technologies?*

Research is at the heart of everything we do. It sparks curiosity, builds independence and gives learners the confidence to think for themselves. At undergraduate level, it's about learning to question evidence, analyse results and make decisions based on facts — essential skills in today's data-driven world. At postgraduate level, research becomes exploration — creating new methods, testing new technologies and pushing the limits of what's possible with AI, digital tools and analytics.

Q: Innopharma Insights *aims to highlight innovations in the digital and technology fields. How does Innopharma stay ahead in these rapidly evolving areas?*

We stay ahead not by chasing every new piece of technology, but by staying curious. Our real strength comes from asking questions — exploring, testing and reflecting with purpose.

Thanks to strong industry partnerships, our faculty bring real-world experience from (Bio)Pharma, MedTech, Food and Digital Transformation straight into the classroom. Learners get hands-on with the same cutting-edge tools — AI, digital tools and simulations — used across global industries. But we also teach them to challenge what they use: to spot bias, to ask *why* and to always think ethically.

Q: *How is Innopharma Education incorporating digital tools and AI in education and research to benefit students and faculty?*

Digital transformation isn't just something we do — it's part of who we are. We use AI and data tools to make learning more personal, giving students instant feedback and in helping them take control of their own progress. In research, digital tools, simulations and predictive analytics let learners explore, test and experiment in ways that just weren't possible before. But it's not only about using new tech — it's about *thinking differently*. We want our graduates to be curious, reflective innovators who know when to trust the data — and when to trust their own judgement.

Q: *Sustainability and responsible innovation are key themes in the journal. How does Innopharma Education integrate sustainability principles in both research and educational programmes?*

Sustainability isn't just a policy — it's a mindset. But what does it really mean? Is it about cutting waste, protecting the planet, or rethinking how we live, learn and lead? At Innopharma, we see it as all of that — and more. Across our programmes, sustainability pushes learners to ask the tough questions: *Can we do this better? Should we do it at all?* It's about balancing innovation with responsibility — making sure progress always has purpose. True sustainability goes beyond the environment. It's ethical, it's human and it's about thinking deeply, acting wisely and creating change that lasts.

Q: *What are the future directions of academic research at Innopharma?*

The future of research at Innopharma is about collaboration, digital innovation and meaningful change. We're building strong partnerships that connect academia and industry, using AI, data and regulatory tech to create smarter, safer and more transparent systems. But innovation on its own isn't enough. Our focus is on progress that's ethical, sustainable and human — research that questions, reflects and genuinely makes a difference. Above all, we're growing a culture of curiosity — where every learner and researcher sees questioning not as doubt, but as the first step toward discovery.

Q: *What do you see as the biggest challenges and opportunities for research at Innopharma Education in the next five years?*

Our biggest challenge is also our greatest opportunity — the speed of change. AI, automation and digitalisation are transforming industry faster than ever, so our research must stay agile, ethical and ahead

of the curve. In a world overflowing with information, real value comes from being able to question, analyse and think for yourself. At Innopharma, we see this as a chance to rethink what research can be — bringing together sustainability, digital transformation and regulatory science to drive innovation that truly matters. With curiosity and courage, we won't just keep up with change — we'll lead it.

Q: *How does Innopharma develop its academic programmes to prepare students for the evolving job market?*

Preparing students for the future means developing thinkers, not just workers. At Innopharma, we build digital confidence, curiosity and agility — the skills that make graduates adaptable in a world of constant change. Through live projects, real industry challenges and cutting-edge tools like AI and digital manufacturing systems, our learners don't just gain skills — they learn to question, analyse and innovate. We don't prepare students to be *job-ready*; we prepare them to be *future-ready* — confident, critical and ready to shape the industries of tomorrow.

Q: *The Innopharma Way is a central pillar in supporting the upskilling and reskilling of learners to prepare them for a dynamic work market. How do you ensure the advice remains contemporaneous to industry?*

The Innopharma Way is about more than developing careers — it's about developing thinkers.

We stay connected to industry, so our teaching, guidance and programmes always reflect what's real and relevant. But our true goal goes deeper: to help people question, analyse and shape their own paths with confidence. In every conversation, project and class, we encourage curiosity — the courage to ask *why* and *what if*. That ability to think critically isn't just a skill for work; it's a lifelong advantage. The Innopharma Way isn't a framework — it's a mindset: curious, adaptable and always evolving.

Closing Comment

"Progress doesn't start with answers — it starts with questions. At Innopharma, we empower people to think critically, challenge assumptions and lead with curiosity and integrity in a constantly changing world."

Finbarr Sheehy

Insights | Showcase - Food Product Innovation: 2025

Author: Jennifer Campbell

Jennifer Campbell is the Programme Lead and Programme Chair for the Food Science and Technology Programmes at Innopharma Education. Jennifer lectures in the areas of occupational and environmental health and safety, risk management, food safety and digital communications and technical writing. Prior to joining Innopharma Education in 2021, Jennifer worked within the food manufacturing industry in companies such as Aryzta Food Solutions and Brennans Bread in QA and Technical roles.

Here, Jennifer offers an insight into our Level 8 Higher Diploma in Food Science and Technology programme, in particular the standout module focused on student led research in food product innovation and development. In this module, students work as teams to create innovative new food or beverage products that are shelf ready, consumer tested and filling a gap in the ever-competitive food and beverage market.

Innopharma Education's *Level 8 Higher Diploma in Food Science and Technology* learners once again delivered an impressive showcase of innovation and expertise at their annual Food Product Innovation and Development presentation event, held at our Sandyford Campus in April 2025.

The event served as the culmination of weeks of collaborative work, where learners were challenged to create unique food products that respond directly to current market trends and evolving consumer demands.

Working in dedicated teams, learners navigated the full product lifecycle, from identifying consumer needs through market research to developing formulations, branding, packaging, and pricing. This comprehensive module equips learners with a blend of scientific, business and innovative skills, ensuring their product concepts were not only creative but also market-ready and commercially viable. Each team's journey concluded with live presentations, during which products underwent rigorous taste testing and assessment by a panel comprised of both academics and food industry experts—an always exciting and rewarding experience for all involved.

Learners presented their products from concept to taste

Industry Support and Real-World Feedback

At Innopharma Education, one of our core aims is to continually strengthen the connection with the Irish food industry. A distinctive feature of this year's event was the valuable collaboration and insight provided by BWG Foods. Orla Kelly, *Head of Food & Beverage Innovation*, and Lisa Garrett, *Range Development and Implementation Manager*, joined the testing panel where they offered learners expert feedback on product viability, scalability and food safety compliance. Their constructive questioning and engagement highlighted the importance of bridging academic learning with real-world industry expectations and rigour, ensuring graduates are well-equipped for Ireland's dynamic food sector.

Orla Kelly, Head of Food & Beverage Innovation, and Lisa Garrett, Range Development and Implementation Manager, joined the testing panel from BWG foods.

Lecturers, Leads and Learners all enjoyed a day of presentations and tasting the products.

Celebrating Learner Achievement

This year's presentations highlighted not only technical expertise and market awareness, but also outstanding professional communication and teamwork. "*The final presentation empowers learners to demonstrate their creativity, critical thinking and ability to deliver shelf-ready food and beverage innovations*", remarked Orla Callan, *Managing Director and President of Innopharma Education*. The event once again underscored the programme's commitment to fostering future food industry leaders who are equipped with the skills to drive progress in a rapidly changing marketplace.

Product Highlights

This year's class delivered an impressive and imaginative array of food innovations, each project reflecting contemporary trends while addressing meaningful consumer needs.

Among the exciting concepts was a vegan, gluten-free oaty churro brought to life by Dominykas, Dariush and Rosihidin. Their reimagining of this popular snack not only captured the growing demand for plant-based and gluten-free treats but also highlighted the influence of new cultures and dietary shifts making their mark on the Irish food scene. The churros offered a delightful and inclusive twist on a classic indulgence, ensuring that more consumers—regardless of dietary restrictions—could enjoy a modern take on this international favourite.

Innovation in premium foods took centre stage as another group comprising Kevin, Margaret and Maurice introduced *Talamh Farraige*, an artisanal seafood pasta sauce. Distinctively flavoured with a signature ingredient, Piment Rouge Combava, this product stood out in a category that market research has shown to be thriving. Both Irish and UK consumers are seeking out next-level takes on the "humble" tomato sauce, with a growing enthusiasm for gourmet and small-batch condiments—a trend

maximised by this group's dedication to both flavour and originality.

Yet, it wasn't just mainstream consumer trends that were represented. Corina, Baptiste and Khristiana identified a gap in the care home and assisted living sector, designing a melt-in-the-mouth almond lemon biscuit specifically crafted for those with chewing and swallowing difficulties such as dysphagia— a thoughtful addition to the classic tea-time ritual within the care home and assisted living sector and a product carefully designed to support residents with specific dietary and texture needs. By combining gentle texture with bright, appealing flavours, the team succeeded in creating a treat as practical as it was pleasing.

The ever-increasing popularity of functional foods and nutritionally enhanced snacks was showcased with *GlowPro*, a collagen-filled protein bite designed to link the global interest in skin health and high-protein diets. Eilish, Shauna & Paul offered a convenient way for wellness-minded consumers to enjoy the benefits of collagen and essential vitamins, all in a snackable format—directly answering the drive for everyday foods that support holistic health.

Seaweed also made an appearance, as Aislinn, Conor, Janki and Justyna embraced sustainability and innovation through the creation of a seaweed tortilla wrap. Their product harnessed the versatile nutritional benefits of seaweed—a food that continues to generate excitement for its role in functional and environmentally responsible eating. By combining it with the familiar format of a tortilla wrap, the team made this superfood accessible to a broad market in a practical, on-trend application.

The Winning Product

Crowning the event was the winning group's CBB—a glazed cottage cheese chocolate bar. Inese, Lucimara and Shane recognised the growing need for snacks that are both indulgent and nutrient-dense. This group elevated humble cottage cheese into a snack that is as wholesome as it is tempting. Their creation struck a memorable balance between health and indulgence, resonating with consumers who refuse to compromise on taste or nutrition.

Recognition and Awards

The event concluded with a celebration of all learner achievements. The creators of CBB, the glazed cottage cheese chocolate bar, received the "Best Food Product Innovation" prize and were praised for successfully fulfilling the project brief by delivering an innovative, shelf-ready retail product with strong market potential. The panel emphasised how the team transformed cottage cheese, an often-polarising ingredient, elevating it to new culinary heights into a nutritious, market-ready snack, highlighting its ability to address gaps in Ireland's health-conscious confectionery sector while excelling in taste and texture. The product's combination of shelf-ready packaging and consumer-centric innovation positioned it as a standout of the day. Their achievement underscored the excellence and ingenuity nurtured by Innopharma Education's Food Product Innovation and Development module.

Insights | Conference Review: BioPharmaChem Impact Conference 2025

Author: Written by Victoria Buckley, based on an interview with attendee Ann Ryan

Ann is the Director of Industry Engagement & Training at Innopharma Education. Ann has over 20 years' experience working in the pharmaceutical industry across various commercial roles and disciplines including microbiology, immunology and veterinary medicines. She is currently completing a PhD, specialising in training effectiveness in regulated environments. Victoria is the Head of Teaching and Learning at Innopharma Education and has worked in education since 2008. Here Ann and Victoria reflect on the BioPharmaChem Impact conference which took place in May 2025.

The 2025 BioPharmaChem Impact Conference and Awards Dinner at Killashee House Hotel, Naas, brought together over 300 leaders and professionals from Ireland's dynamic biopharmaceutical and chemical sectors for a day of sharing insights, collaboration, and celebration.

BioPharmaChem Impact Conference and Awards focused on collaboration and sharing insights.

A Vision for the Future

The event opened with a compelling address from BPCI Chair Joyce Fitzharris, who emphasised the sector's resilience and its vital contribution to Ireland's economy. Fitzharris outlined BPCI's refreshed strategic pillars, focusing on agility, innovation, and a robust talent pipeline — key to Ireland's €116 billion export industry employing 50,000 people directly.

Strategic Themes and Sector Priorities

Key discussions revolved around five strategic themes: quarterly trends and risk analysis, sustainability, digitalisation and AI, ecosystem development and talent initiatives. Advocacy was a major focus, with the BPCI "*Messaging House*" supporting sector-wide communications and effective

lobbying, such as unlocking the National Training Fund surplus for education and research.

Sustainability featured strongly, highlighted by the launch of BPCI's Sustainability Strategy and Responsible Care report, and the formation of a Board-led Sustainability Steering Committee in partnership with regulators like the EPA and HPRA. Digital transformation was also prominent, with a new Digitalisation & AI Steering Group and the BioPharma Business Services Strategy aiming to position Ireland as a global leader in this space.

Talent and Skills Development

BPCI's commitment to talent was evident through a nationwide STEM engagement survey and the expansion of apprenticeship programmes, now offered at four sites. Over 3,000 learners were trained via the BioPharmaChem Skillnet in 2024, reflecting the sector's investment in future-ready skills.

Panel Discussion and Member Engagement

A lively panel discussion, featuring sector leaders including insights from InnoGlobal Technology's Sean Costello, provided a platform for member feedback on BPCI initiatives. The collaborative spirit was clear, with new members welcomed and working groups recognised for their role in benchmarking and best practice sharing.

Celebrating Excellence: The Impact Awards

The evening's highlight was the inaugural BioPharmaChem Impact Awards, recognising excellence across seven categories. For Innopharma, it was a particularly proud moment as Innopharma Technical Services received the "*Best Talent Strategy of the Year*" award—a significant achievement for our team and a testament to our innovative approach to developing and empowering industry-ready professionals through our work simulation programme.

Innopharma Technical Services with their prize for "Best Talent Strategy of the Year"

Conclusion

Other winners included Johnson & Johnson Innovative Medicine (Company of the Year), Astellas Ireland (Sustainability), Boston

Scientific (Collaboration), Sanofi (Process Innovation/Digitalisation), Blynksolve (Emerging Company), and Micro-Bio (Partner/Supplier).

Feedback was overwhelmingly positive, with 98% of delegates rating the event as excellent or very good and a Net Promoter Score of 58, reflecting high satisfaction and loyalty. The conference reinforced the sector's collective ambition and the value of partnership, knowledge-sharing and continuous improvement. For Innopharma, the event was a powerful reminder of our role in shaping the future talent pipeline and supporting Ireland's continued leadership in the life sciences.

Insights | Compliance in Diabetes Digital Health: Ensuring Safe and Effective Insulin Delivery Technologies

Author: George Hove

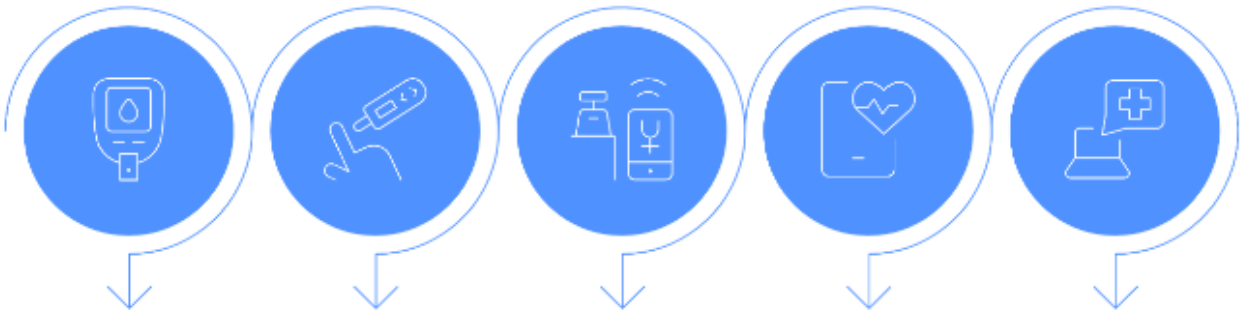
George Hove is a learner at Innopharma Education (BA Honours, Pharmaceutical Business Operations in partnership with Griffith College) and works as a Production Operator in a medical device manufacturing organisation within the pharmaceutical industry. The insights presented in this paper are based on his professional experience and secondary-research.

Introduction

Insulin has been vital in diabetes treatment since its discovery in 1921 by Frederick Banting and Charles Best (Banting et al., 1922). Initially, patients used heavy glass syringes for insulin injections; the introduction of disposable syringes in the mid-1950s made the process much safer and easier for patients. By the 1980s, insulin pens allowed for more accurate dosing and greater convenience. Insulin pumps, used since the 1970s, provided continuous insulin delivery, closely mimicking natural regulation (Pinnaro and Tansey, 2021).

Early Insulin Injection | National Museum of American History

Digital Health Technologies



Continuous Glucose Monitor

Measures blood sugar through a sensor, transmitting real-time data to a mobile app, alerting high or low blood sugar, improving safety and facilitating timely insulin dosing.

Smart Insulin Pen

Connects to mobile applications via Bluetooth, allowing users to track insulin usage and receive reminders.

Automated insulin delivery

Combines CGMs and insulin pumps to monitor blood sugar and adjust insulin doses automatically.

Mobile health applications

Supports users in tracking blood sugar levels, insulin doses, and food intake, offering educational resources, medication reminders, and connectivity with CGMs and smart pens.

Telehealth

Improves access to healthcare by enabling patients to consult providers remotely, allowing for timely insulin management adjustments.

Benefits of Digital Health Innovations

- ***Patient Empowerment***

Continuous glucose monitors (CGMs) and smart insulin pens work with mobile applications to provide near real-time updates on blood sugar levels. This technology empowers patients to manage their diabetes more effectively. Automated insulin delivery (AID) systems further enhance control by automatically adjusting insulin doses based on glucose monitoring (Sherr et al., 2022).

- ***Blood Sugar Control***

A major advantage is improved blood sugar control. Tools like CGMs and AID systems allow individuals to continuously track glucose levels, enabling immediate insulin adjustments. This real-time data stabilises glucose levels and reduces complications (NIDDK, 2023).

- ***Convenience***

Smart insulin pens and pumps simplify administration. Smart pens calculate doses based on blood sugar, while pumps deliver insulin continuously (Lingen et al., 2023). This automation reduces manual calculations and ensures consistent dosing, allowing patients to integrate insulin delivery into daily routines.

- ***Patient Engagement***

Mobile applications encourage users to track blood sugar, insulin, and food intake, often providing educational resources and reminders Active participation improves adherence to treatment plans and health outcomes (Mescher et al., 2024).

- ***Healthcare Accessibility***

Telehealth services allow patients to consult with providers from home, facilitating timely adjustments to treatment plans without travel. This is especially beneficial for individuals in remote areas or those facing challenges accessing traditional healthcare.

Regulatory Landscape

Important Regulations Affecting Digital Health

As digital health technologies evolve, regulations ensure these tools are safe and effective (Smith et al., 2023). Understanding these regulations is crucial for developers, providers, and users. One significant regulation is the Health Insurance Portability and Accountability Act (HIPAA) in the U.S., which sets standards for protecting sensitive patient information. Digital health companies must implement robust data security measures to safeguard patient data. By safeguarding patient data, HIPAA builds trust between users and digital health providers, encouraging more individuals to adopt these innovative tools.

The U.S. Food, Drug, and Cosmetic Act authorises the FDA to regulate medical devices, including digital health tools such as glucose monitors, insulin pumps and diagnostic apps, ensuring their safety and efficacy. In Europe, the Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR) impose stringent standards for device safety, performance, and reliability. As AI and machine learning become integral to healthcare technologies, new frameworks like the EU AI Act aim to govern their ethical and safe application, mitigating risks linked to automated clinical decision-making (Ruggio, 2025).

Compliance Challenges in Digital Health

- ***Data Privacy and Security***
  Wearables and health apps generate extensive personal data, making them prime cyber targets (Crossen et al., 2022). Breaches can cause identity theft and financial harm, underscoring the need for encryption, multi-factor authentication, and frequent audits.

- ***Regulatory Compliance***
  Complex frameworks impose strict controls on data handling. Non-compliance risks fines and loss of trust, prompting investment in legal expertise and systematic compliance policies (DataGuard, 2024).

- ***Interoperability***
  Effective care depends on seamless data exchange among diverse devices and systems (OECD, 2019). Fragmented standards limit integration (Berg, 2024), but frameworks like HL7 FHIR promote harmonisation and patient data portability (Clark & Bailey, 2023).

- ***Validation and Safety***
  Device accuracy underpins clinical reliability (Medical, 2024). Rapid innovation can outstrip regulatory oversight, necessitating rigorous pre- and post-market validation (Mennella et al., 2024). Continuous monitoring, algorithm updates, and training for proper device use are key to ensuring safety and efficacy (Crabtree, 2025).

Strategies for Effective Compliance

Compliance Management in Insulin Devices

Robust compliance systems are essential in insulin delivery and medical device development, ensuring patient safety and regulatory integrity. Effective programs should incorporate clear policies aligned with privacy, safety and quality standards. Regular training fosters a compliance-oriented culture, equipping staff to uphold regulatory and ethical expectations. Transparent reporting channels and leadership endorsement further promote responsible practice. Collaboration with regulatory experts and professional bodies enhances alignment with evolving requirements.

Technology-Driven Compliance Monitoring

Digital tools strengthen compliance through automation, analytics and real-time oversight. Automated systems track regulatory changes and maintain audit-ready documentation, while data analytics detect deviations—such as inconsistent glucose readings—enabling early risk mitigation. Cloud platforms facilitate continuous, cross-team monitoring of clinical and post-market data, supporting faster corrective decisions. Additionally, e-learning systems sustain ongoing staff education, reinforcing regulatory awareness and adaptive compliance across the organisation.

Conclusion and Future Directions

Effective compliance management is vital for companies developing insulin delivery systems and medical devices, ensuring patient safety and fostering trust. A robust compliance program should include clear policies for regulations like data privacy and safety standards. Regular training for employees is crucial, focusing on compliance requirements and ethical practices to create a culture of accountability. Conducting risk assessments helps identify compliance vulnerabilities, while open communication channels encourage reporting of concerns. Collaboration with regulatory consultants enhances compliance efforts in the evolving medical device field. Leveraging technology, such as automated systems and mobile applications, streamlines compliance processes and improves user education. Regulatory technology can automate reporting, reducing administrative burdens. Ongoing education through e-learning keeps staff updated on regulations and best practices. This commitment to continuous learning is essential for maintaining high patient care standards.

The future of digital health is promising, with exciting areas for research and new technologies on the horizon. For instance, artificial intelligence can help doctors make better decisions by quickly analysing patient data. Telehealth is gaining popularity, enabling patients to consult with doctors from home, especially through wearable devices that track health in real time. Blockchain technology may enhance the security of health records, giving patients more control over their information. Additionally, virtual and augmented reality could improve medical training and patient education. These advancements aim to make healthcare more personalised, accessible, and effective for everyone.

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Research Article | Transforming Education Strategies for New Parents on the Measles Vaccine: A Strategic Approach

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Abstract

Measles vaccine hesitancy persists globally. In Ireland, uptake remains at 89%—below the WHO target of 95%—thereby undermining disease elimination efforts.

This study explores parental attitudes, beliefs, and trust during the current measles outbreak in Ireland, aiming to determine which sources new parents rely on for vaccine information and to identify how the pharmaceutical industry could contribute to more effective education strategies.

A mixed-methods design combined an anonymous online survey (n = 103) with Zoom interviews involving 10 new parents and 4 health professionals. Inclusion criteria required participants to be parents of children under two years of age residing in Ireland. Hypothesis testing (n = 101) was conducted in Microsoft Excel.

The results indicate health professionals were the most trusted information source. Hesitancy declined with increased trust in health professionals (r^2=-0.87, $p<0.001$), national health communications (r^2=-0.97, $p<0.001$), and published literature (r^2=-0.97, $p<0.001$). Hesitancy rose with trust in social media (r^2=0.97, $p<0.001$) and was unaffected by trust in news outlets (r^2=-0.05, $p<0.001$) or pharmaceutical companies (r^2=0.21, $p<0.001$).

Thematic analysis identified gaps in vaccine education, a need for campaigns stressing disease risk, stronger legislation against misinformation, and peer-led education. Limited awareness of PRIORIX, a gelatine-free measles vaccine, highlighted poor vaccine literacy.

In conclusion, the pharmaceutical industry can support education by providing clear efficacy and safety data, strengthening training for health professionals, advocating legislative measures to counter misinformation, and promoting vaccine alternatives such as PRIORIX to reduce hesitancy among vegan and vegetarian parents.

Introduction

Despite vaccines being among the most effective tools for preventing infectious diseases, vaccine hesitancy continues to hinder measles elimination worldwide. The World Health Organization (WHO) recommends 95% coverage for herd immunity, yet Ireland remains below 90% uptake (WHO, 2020; HPSC, 2023). Falling short of 95% increases the risk of outbreaks and may reflect gaps in vaccine education and communication. For new parents (NPS), who decide to vaccinate their children, this choice is often characterised by uncertainty (Novilla et al., 2023).

The COVID-19 pandemic heightened public awareness of vaccines (Gallant et al., 2021) but also amplified the spread of misinformation. While NPS can access official sources such as the HSE and HPSC, they are simultaneously exposed to misleading media content (Lewandowsky et al., 2012; Budak et al., 2024), alternative non-scientific evidence exaggerates the risks, fuelling distrust (Kirkedal et al., 2022). The long-lasting influence of Wakefield et al.'s (1998) fraudulent MMR–autism study, despite its retraction, demonstrates how misinformation erodes vaccine confidence (Motta & Stecula, 2021).

Complex and technical pharmaceutical communications further compound the problem. Regulatory data from the European Medicines Agency (EMA), while scientifically rigorous, is often inaccessible to the public (Eller et al., 2019). Consequently, reliable information may seem difficult to interpret, while inaccurate material spreads easily (Smith & Graham, 2019). In this context, parental trust in healthcare providers (HPS), government, and industry becomes central to vaccine acceptance (Williams, 2014).

Ireland's pharmaceutical sector is internationally advanced, supported by academia, investment and state incentives (O'Dwyer et al., 2017; Mullen, 2021). This expertise could support vaccine education, yet EU legislation (Directive 2001/83/EC) restricts direct public communication. Exemptions for state-approved vaccine campaigns provide some scope (European Union, 2021), but effective channels remain underdeveloped.

This study addresses this gap by examining NPS as vaccine decision-makers and HPS as primary educators. It considers how pharmaceutical companies, within regulation, could strengthen measles vaccine education in Ireland.

Literature Review

Measles, one of the most contagious infectious diseases, has been documented since the 9th century and became a global health concern by the 16th century (WHO, 2020). The first vaccine, developed in Boston in 1954 and licensed in 1963, marked a major breakthrough for managing the disease. In Ireland, its introduction in 1985 led to a reduction in annual cases from approximately 10,000 to just over 200 within two years (HPSC, 2024). The MMR vaccine followed in 1988, with a second dose added in 1992. Nevertheless, outbreaks have continued, including 1,248 cases in 1989 and 4,328 in 1993, and coverage remains below the WHO's 95% target for herd immunity (McHale, 2024).

Health professionals, particularly general practitioners and nurses, are the most trusted advisors for parents, offering personalised guidance and reassurance (Barrett et al., 2022). Public health campaigns and school- or community-based programmes have supported uptake, yet vaccine hesitancy and digital misinformation continue to undermine progress (Budak et al., 2024). While authoritative organisations such as WHO, ECDC, and NIAC provide reliable information, competing online narratives often prove more persuasive (Broniatowski, D.A. et al. (2018).

Parental decisions are influenced by perceived disease severity, vaccine benefits, social norms, and—above all—trust in HPS, as conceptualised by the Health Belief Model (HBM) and Theory of Planned Behaviour (TPB). Persistent distrust of pharmaceutical companies, reinforced during the COVID-19 pandemic, highlights the need for transparent communication and strong professional engagement (Leask et al., 2011; Dubé et al., 2013).

Evidence on educational interventions is varied and context dependent. Corrective information alone can be ineffective or counterproductive (Nyhan et al., 2014; Hornsey et al., 2018), while personalised counselling with HPS has been shown to improve acceptance (Gust et al., 2008). The ECDC (2015) emphasises that culturally tailored, locally delivered strategies are typically more effective than mass campaigns. Subgroup-specific models, such as Beverland's (2022) approach for vegan populations, illustrate the value of targeted communication, while legal measures may also be necessary to address misinformation (Caulfield et al., 2017).

Digital platforms both hinder and enable vaccine education. Misinformation is amplified by bots and trolls online (Broniatowski et al., 2018), yet digital reminders, antenatal education, and messaging interventions enhance uptake (Machado et al., 2021). Storytelling and peer advocacy, exemplified by Roald Dahl's appeal following his daughter's death, remain powerful tools for raising awareness (Williams et al., 2014; Gobbo et al., 2023).

Collaboration among HPS, government, and pharmaceutical companies is therefore essential to ensure consistent, credible messaging (Dubé et al., 2013; Jain et al., 2022). Building parental trust through transparency, community engagement, and responsive communication remains critical to improving vaccine confidence. This study applies a conceptual framework adapted from Dubé et al. (2013) and Larson et al. (2015), situating vaccine hesitancy within the "5Cs" model and highlighting the central role of trust in government, HPS, and regulatory authorities (Figure 1).

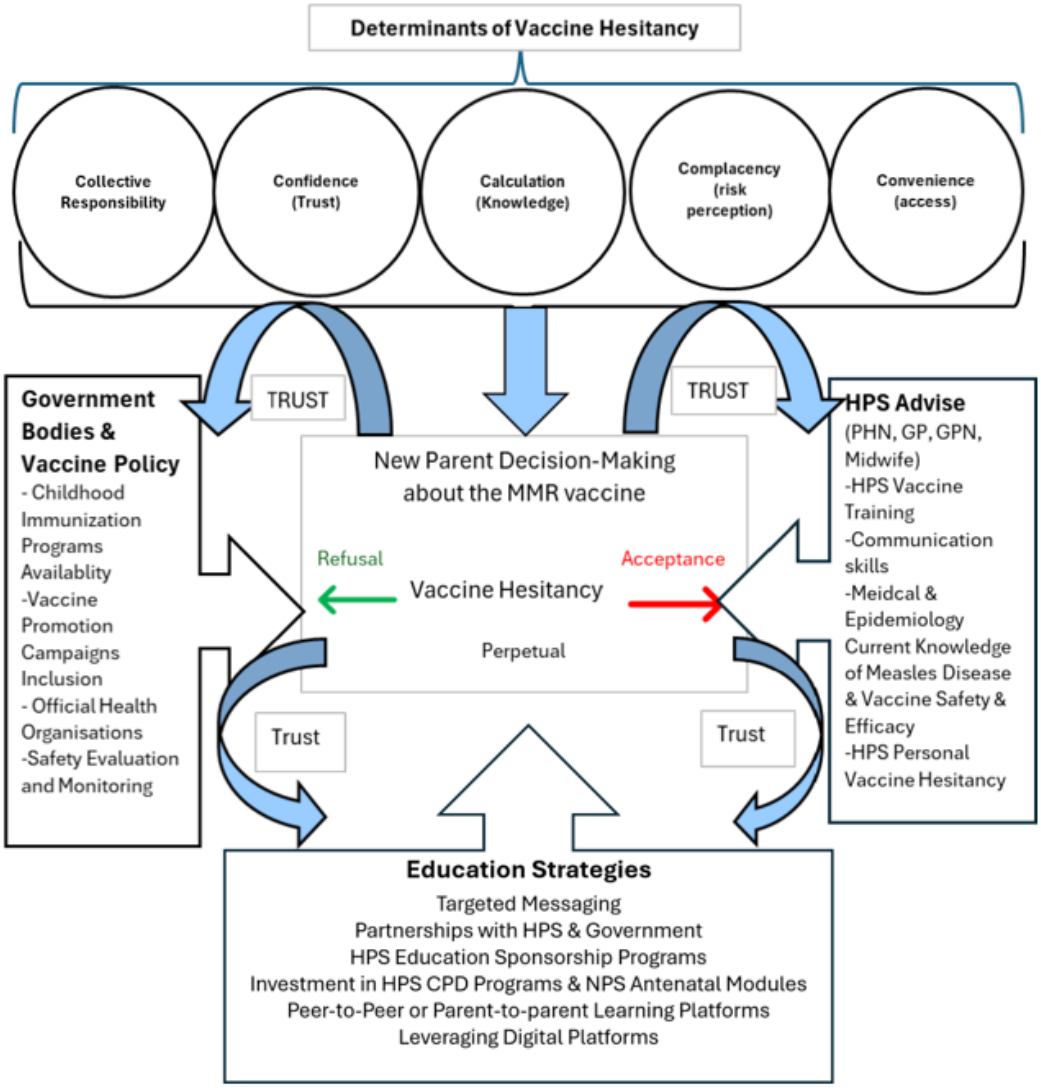

Figure 1: Conceptual framework adapted from Dubé et al., 2013 to include determinants of vaccine hesitancy from Larson et al., 2015.

Methodology

Research Design

A confirmatory research design was employed to investigate the factors underlying measles vaccine refusal in Ireland. A literature review identified key barriers including attitudes, social norms, and risk perception. A survey (n=103) examined immunisation behaviour, trust, and beliefs through mostly quantitative items, supplemented by open-ended questions for thematic analysis. A concurrent triangulation approach was adopted, collecting survey and interview data simultaneously, ensuring complementarity. Semi-structured interviews were conducted with 10 NPS and 4 HPS (Social Worker (SW), General Practice Nurse (GPN), 2 Public Health Nurses (PHN)) to explore trusted sources and preferred education strategies. Open-ended responses from both surveys and interviews were thematically coded.

Data Collection

Survey participants (n=103) were NPS with children under two years, recruited via snowball sampling on social media. While a larger sample (~383) would achieve 95% confidence, this cohort offered timely insights into recent vaccination decisions. Interviews with 10 NPS and 4 HPS provided a deeper understanding of parental rationale, trusted sources, and attitudes toward vaccines, manufacturers, policymakers, and media.

Data Analysis

Survey data were analysed using statistical tests to assess relationships between vaccine hesitancy and trust in information sources, while interviews and open-ended responses were thematically coded to identify patterns in parental beliefs and behaviours. The null hypothesis (H_0) stated: *"Changes in NPS vaccine hesitancy are not affected by trust in information sources."* This was tested across six sources: HPS, social media, news, published literature, national health communication, and pharmaceutical companies, ensuring robust statistical evaluation.

Ethical Considerations

Ethical safeguards were integral to the study design. Participants received clear information about the study, anonymity, and the right to withdraw. Surveys included explanatory paragraphs for informed consent, while interviewees signed consent forms. Interviews were conducted respectfully, allowing participants to elaborate freely.

Results

This study explored Irish NPS perspectives on measles immunisation through surveys (n = 103) and interviews (10 NPS and 4 HPS). Findings revealed limited MMR vaccine literacy: 70% of NPS lacked knowledge of the vaccine's mechanism, 60% were unaware of the MMR1 schedule, and 90% were unaware of WHO uptake targets, highlighting substantial gaps in vaccine education and informed consent.

Parental Beliefs

Parental decision-making on the measles vaccine is driven by child protection (27%), belief in vaccines (21%), disease risk (18%), and HPS recommendations (15%). Among 10 interviewees, 70% described their community as pro-vaccine, though some reported post-COVID hesitancy due to fears of side effects, cognitive issues, or autism. Peer influence and trust in GPs, state bodies, or scientific sources shaped choices. Surveyed NPS (n = 103) were 93–95% non-hesitant, with a strong correlation between general and measles-specific hesitancy (r^2 = 0.97). Most preferred vaccination for immunity (86%), and 64% reported no concerns; among those who did, side effects were the predominant worry. Confidence in the pharmaceutical industry was mixed: 70% trusted it due to regulation and vaccine longevity, while others cited profit motives and past misconduct, noting that distrust had increased since the COVID-19 pandemic.

Information Sources

NPS reported high confidence in HPS (89%), national health communications (90%), and published literature (88%), with low trust in social media (86% disagreed) and neutral scores for news outlets (40%) and pharmaceutical companies (42%).

Responses to Likert-scale questions 15–21 were analysed to assess the relationship between confidence in vaccine information sources and vaccine hesitancy. Statistical tests were conducted at $\alpha = 0.05$. The p-values indicate less than a 5% probability of less than 5% that vaccine hesitancy is independent of confidence in the six information sources tested.

Spearman correlation results revealed a very strong positive association between hesitancy and trust in social media (r^2 = 0.97), suggesting higher trust in social media corresponds to greater hesitancy. Conversely, there is a very strong negative correlation between hesitancy and trust in HPS (r^2 = -0.87), published literature (r^2 = -0.97), and national health communications (r^2 = -0.87),

indicating that trust in these sources reduces hesitancy. Trust in news outlets (-0.05) and pharmaceutical companies (0.21) showed only weak correlations, suggesting minimal influence.

Using Excel's =CHIINV (probability, DF) function, critical values were calculated at 74.22 (α/2 = 0.975) and 129.56 (α/2 = 0.025). These were used to test the null hypothesis (H_0): *vaccine hesitancy is not affected by trust in information sources*. Sigma values were derived from expected standard deviation and Chi-square test statistics, with X values calculated accordingly.

Results indicate that the null hypothesis could not be rejected for pharmaceutical companies, meaning trust in this source does not significantly affect hesitancy. However, the null hypothesis was rejected for the other five sources, confirming that trust in HPS, national health communications, published literature, news outlets, and social media significantly influences vaccine hesitancy. Overall, findings demonstrate that hesitancy is heightened by reliance on social media and reduced by confidence in professional and evidence-based sources.

Null Hypothesis (Ho): Change in NPS level of vaccine hesitancy levels not affected by trust in vaccine information sources				
Information Source	**p-value**	**Spearman Correlation (r^2)**	**Null Hypothesis Test (Ho)**	**Decision**
Health Professionals	1.97E-07	**-0.87**	173.84	Reject Ho
Social Media Outlets	1.97E-07	**0.97**	36.81	Reject Ho
News Outlets	1.14E-27	**-0.05**	132.5	Reject Ho
Published Literature	3.70E-38	**-0.97**	181.42	Reject Ho
National Health Communications	8.35E-38	**-0.97**	179.77	Reject Ho
Pharmaceutical Company	1.09E-26	**0.21**	127.9	Accept Ho

Table 1: Spearman and Chi-square statistical analysis of vaccine hesitancy and trust in vaccine information sources.

All NPS interviewed identified HPS as their primary information source, supported by HSE materials and, to a lesser extent, immunity passports. Both surveys and interviews highlighted the need for clear, factual information in plain language, covering rationale, efficacy, side effects, and disease risks. Preferred communication methods were face-to-face discussions with HPS (100%), leaflets (90%), and government-provided materials (50%), with lower support for pharmaceutical companies (40%) or social media (30%). Family, friends, and television played minor but occasional roles.

Immunisation behaviour

MMR1 uptake in Ireland has risen from 77% in 1999 to 89.4% in 2023 but remains below the WHO 95% target. COVID-19 disruptions contributed to a decline to 89.5%. Among surveyed NPS, 96% intended to vaccinate children with MMR2. Decisions reflected

Health Belief Model (HBM) and Theory of Planned Behaviour (TPB) constructs, with perceived risks, family experiences, and social norms shaping hesitancy or acceptance. Many parents reported a preference for non-confrontational vaccine discussions.

Education strategy

Vaccine education in Ireland is primarily delivered by HPS through staggered and personalised interactions that build trust and counter misinformation. Catch-up campaigns and one-to-one sessions were valued, though post-COVID distrust was observed. Alternative educators included peer support, schools, and community leaders. Group and antenatal sessions allowed accessible, interactive learning, while credible digital tools broadened reach. Stressing disease risks rather than vaccine benefits increased engagement. While most participants supported voluntary vaccination, citing informed choice, mandatory vaccination was viewed as potentially undermining trust.

Discussion

The study and literature indicate that while NPS receive vaccine education, comprehension and retention are limited (Glanz et al., 2013; Interviewees 3, 5, 6, 9, 10). Basic vaccine facts were often not recalled despite prior exposure. Direct pharmaceutical engagement with NPS was not widely supported; however, materials should be user-focused and avoid technical jargon (Dubé et al., 2013; Barrett et al., 2022; O'Leary et al., 2024; Interviewee 3, PHN1).

Survey and interview findings showed improved awareness following national measles outbreak campaigns (Interviewees 5, 9, 10; survey responses 20, 22, 35, 67, 71, 89, 96). Literature notes risk perception may decline once outbreaks subside, influencing vaccine attitudes (Lessler et al., 2016; Marshall, 2020; Barrett et al., 2022). COVID-19 further reduced perceived risk and fostered distrust in government, pharma, and healthcare among some NPS (Gallant et al., 2021; Interviewees 3, 5, 8). Opportunities for pharma engagement during COVID-19 were largely unmet (Achaiah & Subbarajasetty, 2020).

Hesitancy is most pronounced among groups with specific beliefs, including vegans and those who favour naturopathy

(Caulfield et al., 2017; Beverland, 2022). Education should clarify differences between vaccines and supplements, address ethical concerns, and highlight options like gelatin-free PRIORIX (Hamill, 2021; Wellington & Goa, 2003; Interviewee 8). Greater emphasis is also needed on maternal protection, vaccination schedules, and safety reassurance.

Online misinformation remains a significant barrier (Marshall, 2020; Smith & Graham, 2019). Nevertheless, most NPS expressed higher levels of trust in HPS than in online sources, underscoring the need for sufficient HPS capacity to deliver vaccine education (Budak et al., 2024; survey responses 22, 26, 103). Social media has amplified hesitancy, though general sentiment remains broadly pro-vaccine (Broniatowski et al., 2018).

Parent-to-parent education shows potential but remains a sensitive approach; parents may feel judged, particularly after adverse events. Professional dilemmas, such as social workers balancing personal hesitancy with duty, further highlight the need for care in peer-led interventions.

Pharmaceutical companies can contribute within EU Directive 2001/83/EC, Article 88. Ireland, home to over 85 pharma firms including MMR manufacturers, benefits from strong infrastructure (O'Dwyer et al., 2017; Mullen, 2021). Yet NPS expressed scepticism, viewing pharma as profit-driven rather than patient-centred (Interviewees 3, 5).

Study limitations include the decision not to ask directly about child vaccination to preserve objectivity, omission of demographic variables, and misalignment in Survey Question 6. Variability in interview length and limited sample size may also affect reliability. Maternal protection, confirmed by HPS as a key rationale for scheduling, was not reflected in NPS responses, marking a design gap.

Conclusion

Transforming Ireland's measles vaccine education strategy offers an opportunity to improve uptake and reduce hesitancy. This study highlights the potential role of the pharmaceutical industry in supporting healthcare providers (HPS), government agencies and communities through collaborative partnerships and transparent communication.

The research indicates that healthcare professionals are the most trusted source of information for new parents regarding measles vaccination, while parental trust in

pharmaceutical companies has a minimal effect on vaccine hesitancy. Therefore, supporting healthcare professionals is essential to ensure accurate communication.

Parental beliefs play a strong role in shaping vaccination decisions. Campaigns during outbreaks and the longstanding evidence supporting MMR vaccine safety help reinforce public confidence, although misinformation—including false links to autism—continues to persist.

Targeted educational campaigns, accessible government materials and legislation to combat misinformation can help reduce vaccine hesitancy. Pharmaceutical companies can also support these efforts by providing clear, transparent data on vaccine efficacy and safety.

Vaccine literacy among new parents remains limited. Enhanced antenatal vaccine education and CPD for healthcare providers can help address knowledge gaps and counteract misinformation effectively.

It is important to research parental beliefs in depth to tailor education campaigns effectively. Strengthening partnerships between healthcare providers and pharmaceutical companies will aid in delivering accessible, evidence-based information. Developing parent-focused programs, including digital and school-based initiatives, can enhance outreach.

Promoting health literacy and regulating misinformation online are crucial steps. Continuous feedback mechanisms should be used to refine education strategies. Approaches to mandatory vaccination should be cautious, taking into account possible exemptions and maintaining public trust. Ultimately, a transparent, collaborative, and culturally sensitive strategy, led by healthcare professionals and supported by the pharmaceutical industry, can strengthen trust, reduce hesitancy and improve vaccine uptake in Ireland.

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Research Article | Optimising Tinosporaside for Advanced COVID-19 Therapy

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Abstract

This study investigated the antiviral properties of Tinosporaside, a natural compound extracted from *Tinospora cordifolia*, along with its chemically modified derivatives, as a potential treatment approach for COVID-19.

The focus was on two critical viral enzymes, Mpro and PLpro, which were essential for viral replication and immune system suppression. A computational, quantitative methodology was employed instead of a survey-based approach. Techniques such as molecular docking and molecular dynamics simulations were used to design and analyse 56 analogues of Tinosporaside.

Among these, one derivative, T46, demonstrated notably strong and stable binding to both viral enzymes. T46 outperformed the original compound, showing improved drug-like characteristics, including high absorption, low toxicity, and chemical stability.

Structural modifications, such as the incorporation of a pyrrole ring, a carboxylic acid group, and a bromine atom, played a key role in enhancing its antiviral effectiveness. Further simulations confirmed that T46 could effectively interact with both enzyme targets, potentially disrupting the virus's ability to function and replicate.

Overall, the findings suggested that T46 had strong potential as a lead compound for antiviral drug development. While the conclusions were based on computer simulations, they offered a promising foundation for laboratory research and future clinical applications. This work also demonstrated how natural compounds could be refined through modern computational techniques to combat emerging viral threats like COVID-19.

Introduction

Natural products have historically served as the foundation for many modern medical treatments, particularly in the field of infectious disease. A significant proportion of currently approved antiviral medications are either derived directly from natural compounds or inspired by them. This long-standing reliance on plant-based remedies continues to inspire new research in drug discovery, especially in the face of global health challenges such as the COVID-19 pandemic. One such natural compound, Tinosporaside, found in *T. cordifolia*, has gained attention for its known antioxidant, antimicrobial and immunomodulatory properties (Singh *et al.*, 2021). *T. cordifolia* has long been a staple of traditional Indian medicine, and modern science has begun to uncover the molecular basis of its therapeutic effects (Khan *et al.*, 1989). With the ongoing emergence of SARS-CoV-2 variants and the limitations of current antiviral drugs, particularly for vulnerable populations, there is an urgent need to identify new, more effective therapeutic candidates (Focosi *et al.*, 2025).

This study addresses the need for more effective antiviral treatments against evolving SARS-CoV-2 strains (COVID-19), as current therapies often lose effectiveness due to viral mutations and limited target specificity. Many existing drugs fail to inhibit multiple viral mechanisms, reducing their ability to combat replication and resistance. Targeting both the main protease (Mpro, PDB ID: 7ALH) and papain-like protease (PLpro, PDB ID: 6WX4), essential enzymes for viral survival, offers a promising dual-inhibition strategy. The objective is to assess the antiviral potential of Tinosporaside and its chemically modified analogues using *in silico* techniques, including molecular docking, molecular dynamics (MD) simulations and ADMET predictions. The goal is to identify derivatives with improved binding affinity, pharmacokinetics and drug-likeness, potentially outperforming the parent compound as safer and more effective antiviral candidates.

This research holds significance for accelerating antiviral drug discovery by combining traditional plant-based medicine with advanced computational methods. It also promotes sustainable drug development through Computer-Aided Drug Design (CADD), which reduces time, cost, and environmental impact. The findings could contribute to the global fight against COVID-19 and support the development of versatile therapeutics for future viral outbreaks.

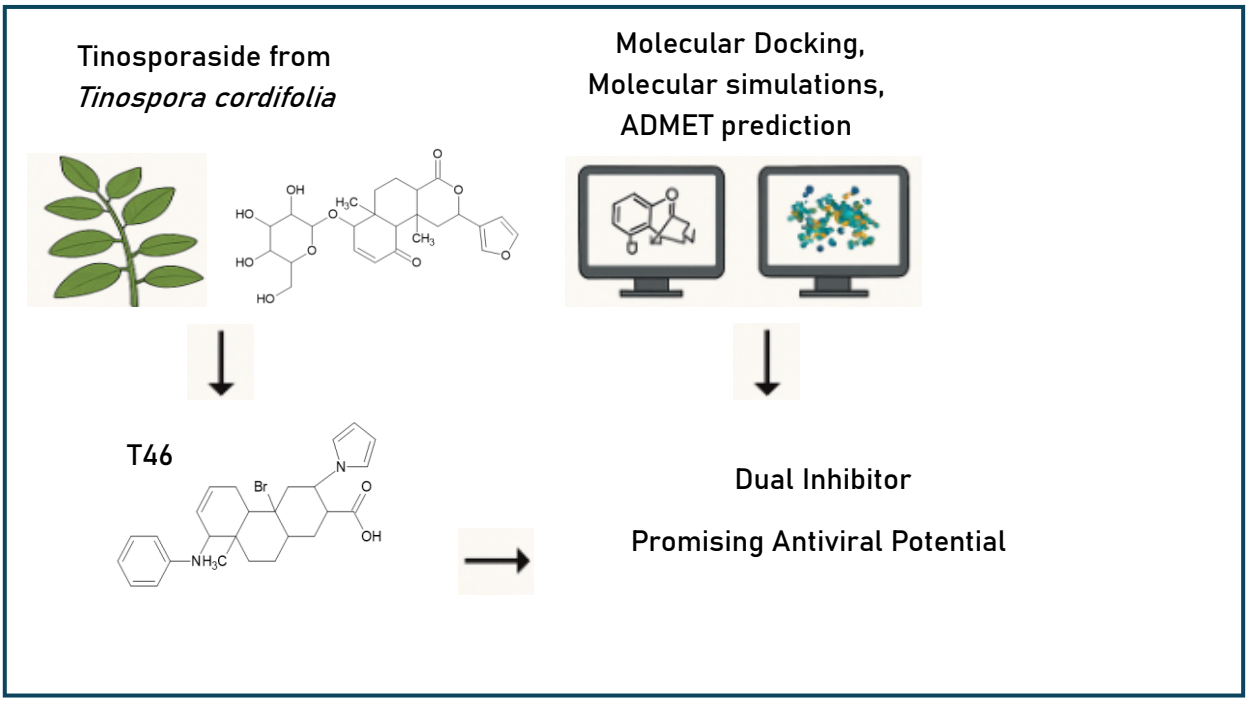


Figure 1: Illustration of Tinosporaside's modification into T46 and its evaluation through computational methods as a potential dual antiviral inhibitor.

Literature Review

SARS-CoV-2 and Global Health Impact

SARS-CoV-2, the virus responsible for COVID-19, emerged in late 2019 and rapidly evolved into a global pandemic. Initially linked to a seafood market, its origins remain under investigation, with animal-to-human transmission considered most likely (Plummer, 2024). The disease has caused widespread health, social, and economic disruptions. The World Health Organization (WHO) emphasised transparency and global cooperation to mitigate future pandemics, particularly as new variants continue to emerge (WHO, 2020). Ongoing genomic surveillance has identified rapidly spreading variants like Eris and KP.3, highlighting the urgent need for adaptive therapeutics (ECDC, 2025).

Viral Proteases: Mpro and PLpro as Therapeutic Targets

SARS-CoV-2 depends on protease enzymes, mainly Mpro (3CLpro) and PLpro, for replication. These enzymes cleave viral polyproteins into functional units required for transcription and assembly (Grum-Tokars *et al.*, 2008; Báez-Santos *et al.*, 2015). Their structural conservation across variants and lack of human homologs make them ideal antiviral targets with a lower risk of side effects (Mukherjee and Dikic, 2023). Mpro's catalytic dyad (His41 and Cys145) and PLpro's immune-modulatory activity are critical for viral survival, making them central to drug development efforts (Báez-Santos *et al.*, 2015; Liu *et al.*, 2020).

Natural Compounds in Antiviral Therapy

Natural compounds, particularly plant-derived bioactives, have long been explored for antiviral activity. Compounds like flavonoids, terpenoids, and polyphenols may inhibit viral entry and replication (Atampugbire *et al.*, 2024). However, despite promising *in vitro* results, few have undergone clinical validation for SARS-CoV-2 (NCCIH, 2022).

Computational Drug Discovery and Molecular Optimisation

Computational tools such as AutoDock Vina, iMOD, SwissADME and ProTox enable virtual screening, binding affinity prediction, simulation and toxicity profiling (Trott and Olson, 2010; Lopéz-Blanco *et al.*, 2011; Daina *et al.*, 2017; Banerjee *et al.*, 2024). These *in silico* methods have accelerated the identification of potential inhibitors but still require experimental validation. Structure-Based Drug Design (SBDD) and

molecular modification techniques can improve compound stability, potency, and drug-likeness, but predicting *in vivo* performance remains a limitation (Nadendla and Yemineni, 2024).

Research Gap and Justification

Despite progress, there is a lack of effective, broad-spectrum antiviral agents targeting conserved SARS-CoV-2 enzymes. Natural compounds like Tinosporaside are underutilised and require further structural refinement and validation. This study addresses these gaps by integrating computational modelling, protease targeting, and natural product research to develop novel antiviral leads (Chowdhury, 2020; Tumskiy *et al.*, 2023).

Methodology

Research Design

This research adopted a computational drug discovery approach to identify and evaluate potential antiviral compounds targeting SARS-CoV-2 proteins. Unlike traditional experimental techniques, this *in silico* method relies entirely on digital simulations, offering a rapid, cost-effective, and resource-efficient workflow critical in responding to urgent global health challenges. The research followed a quantitative, deductive methodology under a positivist paradigm**.**

The rationale for choosing this method is rooted in its efficiency and alignment with green chemistry principles. Computational drug discovery allows virtual screening and detailed molecular interaction predictions without generating physical waste. Tools such as molecular docking and MD simulations provide atomic-level insights into protein-ligand interactions, enabling predictions of binding affinities, stability and drug-likeness with significant precision.

Target Protein Selection

Two key viral proteins, Mpro (7ALH) and PLpro (6WX4), were selected as drug targets due to their essential role in viral replication. Their high-resolution structures were sourced from the Protein Data Bank and subjected to structural quality assessment and secondary structure analysis using tools like SOPMA and ProtParam. Both proteins showed high stability and were thus deemed suitable for docking studies.

Ligand Selection & Design

Tinosporaside**,** a bioactive compound from *T. cordifolia*, was selected as the lead molecule. Using ChemSketch, 56 derivatives (T1–T56) were designed by

modifying functional groups to enhance antiviral potential. These molecules were screened for drug-likeness using SwissADME based on Lipinski's Rule of Five (RO5), ensuring only compounds with favourable oral bioavailability progressed.

Protein & Ligand Preparation

Protein structures were cleaned in BIOVIA Discovery Studio to remove water molecules and extraneous ligands, then processed in AutoDock Tools (ADT) for hydrogen addition and charge assignment. Ligands were similarly prepared, optimised, and converted into PDBQT format for docking.

Molecular Docking

Docking simulations were conducted using AutoDock Vina, guided by grid box coordinates identified via DeepSite. A command-line batch docking process evaluated each ligand's binding affinity with both proteins. Benchmarking was performed using known inhibitors like Nirmatrelvir and PF-07957472 to validate docking results.

Interaction Profiling

The top-scoring complexes were visualised and analysed in PyMOL and Discovery Studio, with interaction profiling done through PLIP to identify hydrogen bonding and hydrophobic contacts.

ADME and Toxicity Assessment

Compounds showing strong interactions were further evaluated for toxicity and ADME properties using SwissADME, pkCSM, and ProTox-3.0.

Stability Analysis

Finally, structural stability of the best protein-ligand complexes was assessed using iMODS, which conducted Normal Mode Analysis (NMA) to measure parameters like B-factors, deformability, and eigenvalues, offering insight into the behaviour of complexes under physiological conditions.

Together, this integrated digital workflow enabled rapid screening, interaction analysis, and safety profiling of potential COVID-19 treatments. The methodology not only reflects the growing role of computational biology in drug discovery but also showcases how *in silico* methods can support rapid response during pandemics and future global health emergencies.

Results

Optimised Tinosporaside and its derivatives as potential therapeutics targeting two SARS-CoV-2 proteases through comprehensive computational analysis.

Protein Target Characterization

The SARS-CoV-2 Mpro (PDB ID: 7ALH, Chain A) and PLpro (PDB ID: 6WX4, Chain B) were selected as primary targets. Physicochemical analysis using ProtParam revealed GRAVY scores of –0.019 for Mpro and –0.433 for PLpro, indicating both proteins are hydrophilic and stable, favouring interaction in aqueous environments. Secondary structure prediction via SOPMA supported their structural integrity and suitability for docking and MD simulations.

Ligand Library and Modifications

A total of 56 structurally modified derivatives of Tinosporaside (T0) were developed using ChemSketch. These compounds were modified through functional substitutions, ring openings, halogenation, and incorporation of antiviral pharmacophores (e.g., favipiravir, remdesivir, tipranavir).

Drug-Likeness Evaluation

SwissADME was used to evaluate all 56 compounds against Lipinski's RO5. Ten compounds failed to meet at least three of the four criteria and were excluded. The remaining forty-six compounds proceeded to docking studies. PAINS filters and GI absorption predictions were also conducted to assess suitability for oral administration. One of the modified structures, T46, uniquely showed high GI absorption and passed all RO5 criteria.

Molecular Docking and Binding Affinity

AutoDock Vina was used to perform molecular docking of 46 compounds with both Protein A (Mpro) and Protein B (PLpro). T0 exhibited binding affinities of –8.5 kcal/mol (Protein A) and –8.9 kcal/mol (Protein B), which served as thresholds for identifying superior candidates. Thirteen compounds outperformed T0 with both proteins, were taken for further analysis.

Protein-Ligand Interaction Analysis

BIOVIA Discovery Studio visualised 2D/3D docking interactions. T0 showed interactions with residues such as MET A:49, GLU A:166, and GLN A:189 in Protein A. T46 demonstrated enhanced interaction with the protease's catalytic dyad (CYS A:145–HIS A:41) along with stable binding to surrounding residue.

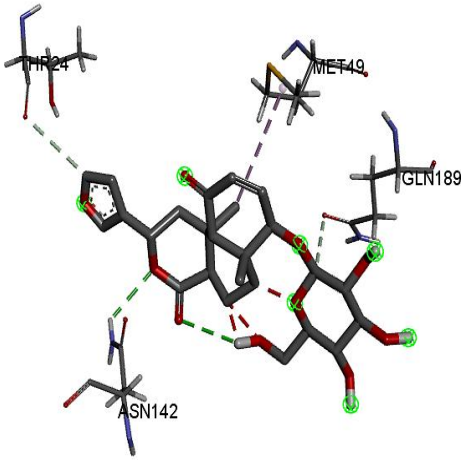
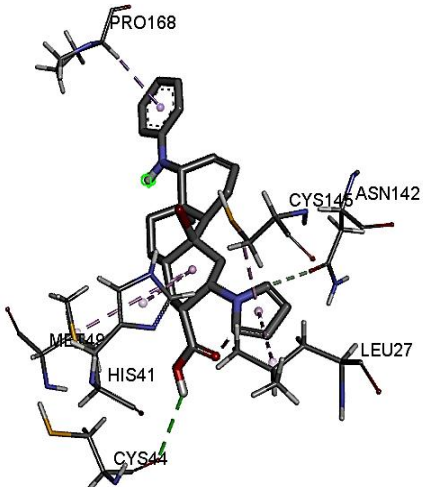
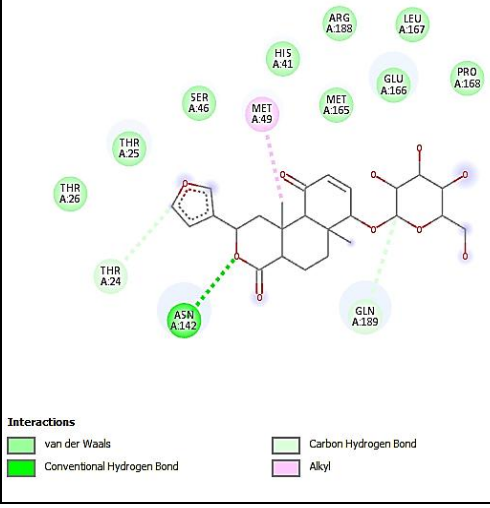
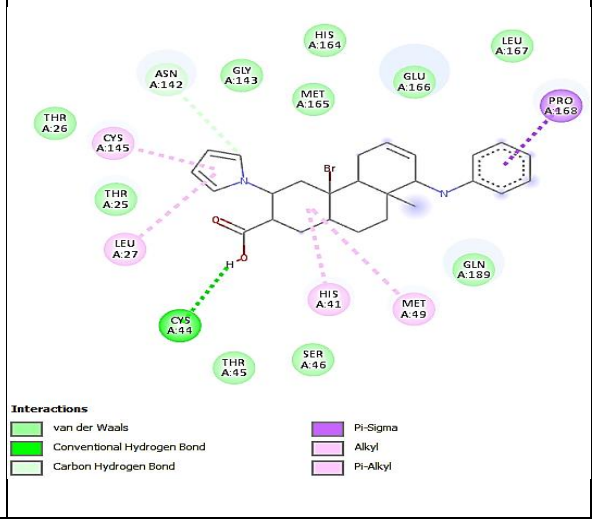
Structure	Tinosporaside (T0)	Modified (T46)
3D		
2D		

Table 1: Three dimensional and two dimensional illustration of the compounds with Protein A

With Protein B, ligands, including T0, did not bind to the catalytic triad (CYS111, HIS272, ASP286) but instead engaged with residues such as Glu143, Ala145, and Phe258, suggesting allosteric inhibition. Further stabilisation occurred via polar residues like Lys91, Glu214, and aromatic residues such as Trp93.

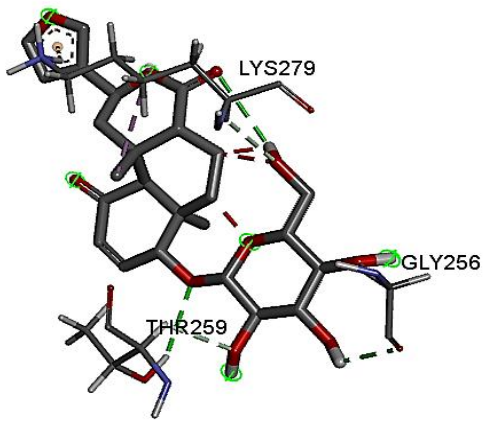
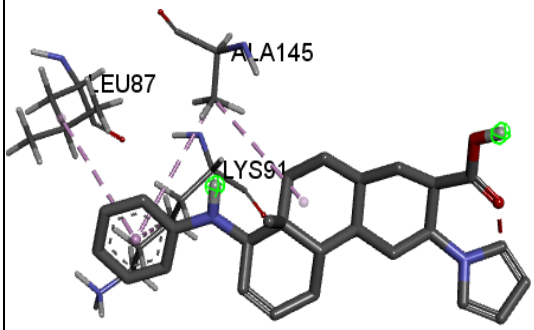
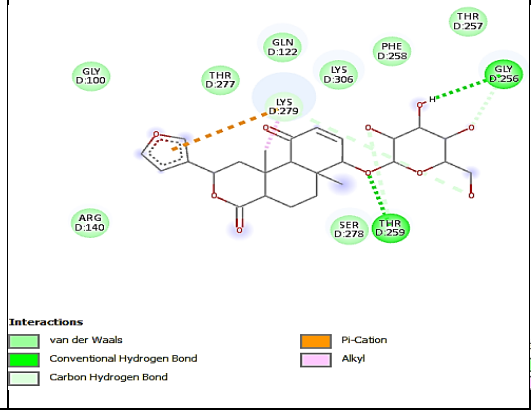
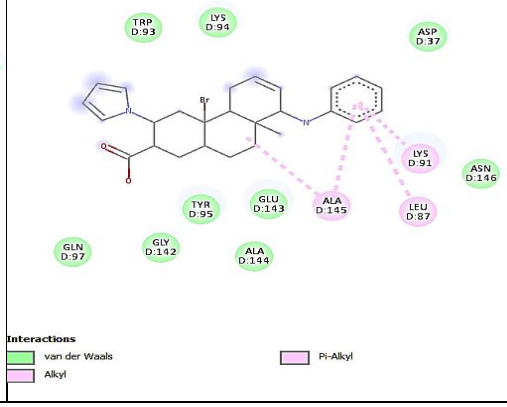
Structure	Tinosporaside (T0)	Modified (T46)
3D		
2D		

Table 2: Three-dimensional and two-dimensional illustration of the compounds with Protein B

Five compounds (T11, T12, T27, T31, T36) exhibited unfavourable interactions such as steric clashes or donor–donor overlaps—and were removed from further consideration. The remaining eight compounds proceeded to interaction refinement.

Hydrogen and Hydrophobic Interaction Profiling

PLIP analysis identified consistent hydrogen bonding in Protein A (GLU A:166, ASN A:142) and strong hydrophobic contacts in Protein B (THR D:259, LYS D:279). T46 and T8 also displayed halogen bonding, enhancing binding stability.

Toxicity Assessment

Toxicity profiles from pkCSM and ProTox-3.0 indicated that T0 was moderately toxic (Class 3), showing multiple organ toxicities. Among the derivatives, T46 stood out with a non-toxic profile (Class 6) and improved GI absorption. Four other derivatives shifted to Class 4, showing moderate improvement, while others remained in Class 3.

Pharmacophore Analysis and Lead Identification

Most derivatives retained the diterpenoid-lactone scaffold, which correlated with persistent toxicity and low absorption. T46 presented a distinct pharmacophoric framework with three fused six-membered rings, a pyrrole moiety, a bromine substituent, and a terminal COOH group resembling a steroid-like architecture.

MD Simulation

NMA using iMOD showed that T46 binding increases flexibility in distinct regions of each protein. In Protein A, the main flexible areas are in two separate regions toward the beginning and middle of the structure, while in Protein B they are found in regions toward the beginning and closer to the centre. In both cases, most movement is driven by a single low-energy motion, but the positions of flexible regions differ. Notably, covariance and elastic network analysis indicate that T46 binding may trigger allosteric effects in Protein B, while such effects were not observed in Protein A. The strong agreement between simulated and experimental data supports the reliability of these findings.

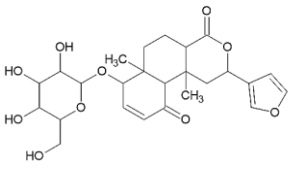
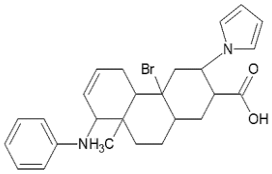
Molecular Profile	Tinosporaside (T0)	Modified (T46)
Chemical Structure		
Modifications	0	➢ A bromine atom (Br) attached to one of the rings. ➢ A methylated amine group (-NH-) attached to a phenyl ring. ➢ COOH group attached one of the rings ➢ A pyrrole ring fused or connected to the steroid core. ➢ Removed CH3 groups, ketones, glucose, lactone ,furan ring
Lipinski rule	YES	YES
Binding Affinity (kcal/mol)	Protein A- (-8.5) Protein B- (-8.9)	Protein A- (-8.7) Protein B- (-8.9)
Type of Interaction	Protein A- Active site Protein B- Allosteric site	Protein A- Active site Protein B- Allosteric site
Toxicity Class	Class 3 (Harmful)	Class 6 (Non-toxic)
GI absorption	Slow	High

Table 3: Comparison of Molecular profile of T0 and T46

Discussion

The findings of this study underscore the potential of computational drug design in optimising natural compounds against viral targets. Tinosporaside, a naturally derived molecule, demonstrated moderate inhibitory potential against SARS-CoV-2 proteases. However, its limited GI absorption, high toxicity, and non-specific binding prompted the exploration of modified derivatives.

Through strategic chemical modifications targeting antiviral enhancement and pharmacokinetic improvement, 56 derivatives were developed. Structural edits, including furan replacements, glucose removal, and addition of heterocyclic pharmacophores, were designed to improve binding, selectivity, and metabolic stability. Despite these efforts, only 46 compounds complied with Lipinski's RO5, illustrating the challenges in balancing potency with drug-likeness.

Molecular docking analysis proved pivotal in identifying lead compounds. Thirteen derivatives surpassed the reference T0 in terms of binding affinity with both SARS-CoV-2 Mpro and PLpro. Importantly, compounds such as T46 engaged catalytic residues, suggesting a competitive inhibition mechanism. In contrast, PLpro binding appeared to rely on allosteric inhibition, as ligands interacted with non-catalytic but stabilising residues.

The exclusion of five derivatives due to unfavourable binding interactions highlighted the importance of spatial compatibility and hydrogen bonding orientation in drug-target engagement. Further refining these molecules through structure-based design or conformational adjustments may enhance their performance.

Among the remaining eight candidates, T46 emerged as the most promising. It's unique scaffold, including a pyrrole-linked phenyl group and bromine substitution, represents a departure from the diterpenoid-lactone core retained in other compounds. This new pharmacophore demonstrated superior protein engagement, improved toxicity classification, and better oral bioavailability.

The molecular dynamics simulations provided further validation. T46 binding induced coordinated flexibility in both proteins, which may reflect functional modulation of the enzymatic sites. The NMA results suggest that T46 not only binds effectively but may also influence protein

conformation, possibly enhancing inhibitory outcomes.

Nevertheless, several challenges remain. Despite toxicity improvements in some compounds, residual immunotoxicity and respiratory toxicity were observed. Additionally, most compounds lacked significant blood–brain barrier permeability, which is acceptable for non-CNS COVID-19 treatments but could limit broader therapeutic application.

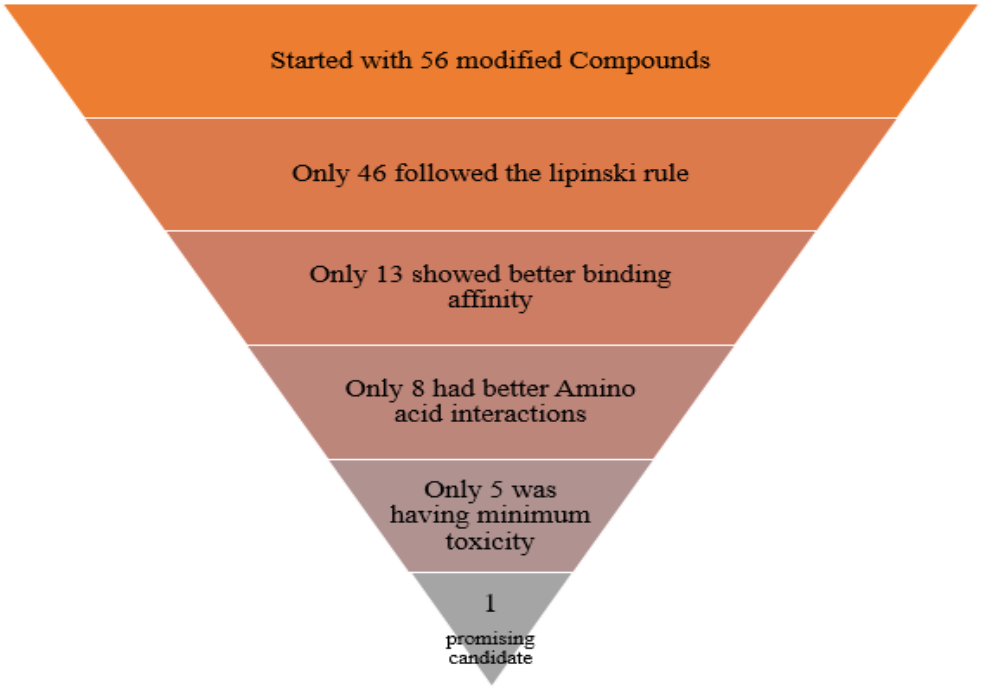


Figure 2: Funnel diagram showing the filtering of 56 modified compounds.

In summary, this study successfully narrowed a large library of modified Tinosporaside derivatives to a single lead compound, T46. It's superior binding, safety, and structural uniqueness make it a strong candidate for further preclinical evaluation, including *in vitro* assays and ADMET profiling. Future work should aim at optimising this scaffold to further reduce toxicity and improve pharmacokinetics, advancing it toward therapeutic viability against COVID-19 and potentially other viral diseases.

Limitations

The findings presented in this study are based on predictive *in silico* models and therefore require biological validation to confirm their relevance. While protein conformational flexibility was considered in the simulations, it was only partially addressed, which may limit the accuracy of predicted interactions. Furthermore, only a limited set of chemical modifications was explored, and a broader assessment of structure–activity relationships could potentially yield more potent derivatives. Finally, although open-source computational tools provided a cost-effective platform for analysis, their precision may be lower compared to proprietary software solutions.

Conclusion

This research systematically explored the antiviral potential of Tinosporaside (T0) and its derivatives against SARS-CoV-2 through *in silico* analysis, with emphasis on the dual inhibition of the viral proteases Mpro (7ALH) and PLpro (6WX4). Among fifty-six designed analogues, T46 emerged as the lead compound, showing superior dual-target binding affinity, improved pharmacokinetic properties, and no predicted toxicity. Structural modifications such as the addition of a steroid-like scaffold, a pyrrole ring, a -COOH group and bromine substitution were critical in enhancing solubility, selectivity, metabolic stability, and overall drug-likeness.

Molecular docking and dynamics simulations confirmed the stable binding of T46 to both catalytic and allosteric sites, inducing conformational changes that may reduce protease activity. The pharmacophore shift from T0's diterpenoid-lactone core to T46's modified structure significantly improved interaction specificity and bioavailability. These findings successfully addressed the research objectives by identifying a novel Tinosporaside derivative with strong potential as a dual-target antiviral agent, providing critical structural and mechanistic insights for future drug design, and establishing a foundation for preclinical evaluation of T46 and related compounds. The results not only fill an existing gap in phytochemical research on Tinosporaside but also position T46 as a strong framework for developing multi-target antiviral therapies, which could play a vital role in reducing viral replication and resistance.

To advance these findings from computational predictions toward

therapeutic applications, several recommendations are proposed. The use of advanced computational tools should be integrated to refine interaction predictions and assess long-term binding stability. Synthetic optimisation strategies need to be developed to enable scalable, cost-effective production for preclinical and clinical studies. Mechanistic studies should be conducted to better distinguish viral-targeted activity from potential host interactions, thereby enhancing specificity. In addition, broader structural exploration is recommended to discover further chemical modifications capable of improving potency and bioavailability. Finally, experimental validation through both *in vitro* and *in vivo* assays will be essential to confirm the inhibitory efficacy and safety of T46, ultimately driving the development of this compound into a viable therapeutic candidate.

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Research Article | Digitalisation of Functional Outcome Assessments in Clinical Trials: Integrating Cardiac Activity Sensors into the 6-Minute Walk Test

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Abstract

The increasing digitalisation of clinical trial assessments holds great promise for enhancing the reliability, accuracy, and patient-centricity of outcome measurements. This research investigates the feasibility, advantages, and challenges of incorporating wearable cardiac activity sensors—specifically consumer-grade devices such as the Apple Watch—into the established 6-Minute Walk Test (6MWT), a key functional assessment in trials for cardiovascular, pulmonary, and neurological diseases.

Through a dual-arm study comprising a feasibility pilot with healthy adults and an expert survey of pharmaceutical industry professionals, the research assesses both practical patient-side considerations and the perspectives of key industry stakeholders. Findings indicate that digital devices can strengthen data quality, automate collection of additional clinically relevant metrics, and support more flexible, decentralised trial models.

However, significant barriers remain; technical malfunctions, data privacy concerns, integration with existing workflows, budget and compliance issues, and unresolved clinical validation questions. Experts highlight the need for targeted training, robust technical support, and careful management of regulatory, ethical, and patient selection issues.

This article demonstrates both the transformative potential and complex implementation landscape of sensor-based digitalisation in outcome assessments, providing actionable recommendations for stakeholders seeking to modernise clinical trials while optimising patient safety and data integrity.

Introduction

Healthcare and clinical research are undergoing a digital transformation, fundamentally altering the collection and utilisation of health data. A central challenge in both domains remains the reliable and reproducible assessment of functional status, particularly in trials targeting chronic and progressive diseases such as heart failure and pulmonary arterial hypertension (PAH). The 6-Minute Walk Test (6MWT) has long served as a gold-standard field test for submaximal exercise capacity for these conditions along with dilated cardiomyopathy (DCM), valued for its simplicity, cost-effectiveness and strong correlation with morbidity and healthcare utilisation.

Despite the test's widespread uptake, manual administration and endpoint recording introduce sources of human error, inter-rater variability and logistical constraints—notably for remote or mobility-impaired participants. In parallel, digital health technologies and wearable devices are rapidly gaining ground as tools for scalable collection of objective health data, including cardiac parameters, physical activity and event detection. The Apple Watch and similar consumer-grade cardiac activity monitors enable accessible, real-time physiological data capture, opening the door to digital biomarkers that can supplement or refine traditional clinical endpoints.

Adoption of digital tools into established clinical assessments such as the 6MWT could improve data fidelity, enhance patient engagement and foster novel decentralised trial models. Nevertheless, integration is not without challenges: device reliability, data standardisation and privacy, workflow adjustments and regulatory hurdles all require careful management. There is a paucity of empirical research exploring both "real-world" participant experiences and the nuanced perspectives of multiple stakeholders along the digitalisation pathway.

This article seeks to address this gap via a two-part study. First, it assesses the technical feasibility and user experience of integrating the Apple Watch into the 6MWT among healthy adults. Second, it collates feedback from pharmaceutical industry professionals on perceived benefits, barriers and risk management strategies associated with the digitalisation of outcome assessments. By synthesising insights across participant and stakeholder groups, this research delivers a critical evaluation of the readiness, challenges and future

trajectory for digitising functional assessments in clinical trials.

Literature Review

Functional Assessments and the Value of the 6MWT

Developed in the late 20th century, the 6MWT quantifies the distance an individual can walk in six minutes, serving as a submaximal measure of aerobic capacity and functional status (Enright, 2003; ATS, 2002). Its utility is well-established for monitoring patients with cardiopulmonary, neurological, and musculoskeletal conditions across the age spectrum, from paediatrics to older adults (Lammers et al., 2008; Troosters et al., 1999). The test's ecological validity, ease of implementation, and predictive value for morbidity and mortality have led to its widespread adoption in both clinical practice and pharmaceutical research to establish baseline function, monitor disease progression, and assess treatment effects (Busch et al., 2023).

Emergence of Digital Biomarkers and Wearable Devices

Digital health technologies have ushered in a new era for the measurement and monitoring of clinical outcomes. Digital biomarkers, which are objectively measured, health-related data from digital devices, offer continuous, real-world insights into disease state and trajectory (Carlos & Josephs, 2023). Wearable technology, typified by devices such as the Apple Watch, enables unobtrusive capture of heart rate, ECG, activity metrics and other physiological signals (Wicks et al., 2019). Their adoption is accelerating in chronic disease management for cardiac, pulmonary, and neurodegenerative conditions, with early evidence suggesting improved event detection, remote patient monitoring, and richer phenotyping (Cowie et al., 2021; Amir et al., 2021).

Clinical Trials and the Digital Shift

Digital health tools are increasingly leveraged in trials to support remote participation, lessen participant burden and enhance the granularity of data collection (Dorsey et al., 2020). Regulatory bodies, including the FDA and EMA, have begun to provide frameworks for the qualification of digital endpoints and the standardisation of software as a medical device (SaMD), although open questions persist regarding data validity, privacy, and equitable access (Food and Drug Administration, 2022).

Evidence and Gaps: Wearables in Functional Assessments

Prior research shows that consumer-grade wearable devices can accurately track physical activity parameters (e.g., step count, distance), and in some cases, cardiac rhythms during functional tests like the 6MWT (Busch et al., 2023). However, concerns remain about their technical reliability under test conditions, patient uptake and familiarity, integration into clinical workflows, and the implications for regulatory submission and inspection (Dorsey et al., 2020; Cowie et al., 2021). Studies to date have largely been conducted in controlled settings or focus solely on technical validation, with a relative dearth of implementation research spanning diverse stakeholder perspectives.

Methodology

Research Design

A mixed-methods approach was undertaken comprising of two distinct but complementary phases:

Part A: A prospective feasibility pilot evaluating sensor integration into the 6MWT in healthy adults.

Part B: A cross-sectional survey with pharmaceutical industry experts familiar with digital health technologies and the 6MWT in clinical research.

Participants and Recruitment

Part A: Ten healthy adult volunteers (convenience sample) were recruited from the professional network of the researcher. Participants committed to weekly 6MWT assessments over four weeks.

Part B: Thirteen pharmaceutical professionals with experience in clinical trial design, safety, digital innovation, or biostatistics participated via survey. Sampling reflected roles in drug development, digital health, and clinical operations with a range of 2–24 years' industry experience.

Intervention and Data Collection

Part A: Each participant completed a baseline and final 6MWT. Walk test parameters (distance, speed, cardiac activity) were captured via the Apple Watch, in parallel with observer logging. User feedback on device wearability and experience was collected after the final session via online, anonymous surveys.

Part B: Experts completed a structured survey addressing perceived benefits, technical and operational risks, ethical considerations and recommendations for

implementation of wearable sensors in the 6MWT and analogous settings.

Data Handling and Analysis

Quantitative metrics (distance, heart rate, compliance rates) were evaluated for technical feasibility.

Qualitative data—open survey responses—were thematically coded to identify benefit-risk themes, perceived barriers and enabling factors.

Summary statistics were derived for challenge frequency and the distribution of expert themes.

Ethical Considerations

Written informed consent was obtained for all study activities. Data were anonymised, retained in accordance with GDPR guidelines and solely used for research purposes as outlined in participant information materials.

Results

Feasibility and Patient Experience (Part A)

Compliance and Data Completeness

All ten participants completed the required sessions; device data were successfully captured in most walks.

Technical Performance

The Apple Watch reliably recorded step count, heart rate, and walking distance in >90% of trials. Occasional technical issues—such as device syncing errors—necessitated repeated assessment but did not preclude data collection.

User Experience

Participants rated the device as generally comfortable and unobtrusive, with minor complaints about fit and the need for charging/preparation. Most indicated willingness to participate in digitally enabled assessments outside a traditional clinical setting.

Job Title / Functional Area	Years of Experience (Pharmaceutical Industry)
Director	11
Digital Innovation Manager	9
Associate Director – Risk Based Monitoring	8
Director, Digital Health Innovation	20
Head of Translational and Experimental Medicine	10
Sr. Manager Biostatistics	13
Digital Health Capability Lab Lead	2
Product Director, Digital Health	6
Associate Director, Portfolio Data Lead	24
Medical Monitor /Clinical Development	3
Medical Monitor	3
MD, PhD, Head of Global Clinical Development	18
Associate Director Risk Based Quality Management	19

Table 1: Expert Stakeholder Perspectives (Part B)

Five perceived benefits emerged from these findings (thematic synthesis):

- *Enhanced Data Accuracy and Fidelity*

  Digital sensors reduce human error, improve standardisation, and allow for more nuanced analysis (e.g., heart rate variability, recovery slope).

- *Automated, Additional Data Collection*

  Collection of heart rate, arrhythmia detection, walking speed, and even movement patterns not possible via manual 6MWT alone.

- *Remote and Flexible Assessments*

  Enable assessments outside clinical sites, supporting decentralised/virtual trial models, reducing travel burden, and fostering inclusivity for less mobile and remote patients.

- *Improved Patient Engagement*

  Real-time progress tracking increases participant motivation and study retention.

- *Data for Clinician Insight*

  Additional metrics can improve disease monitoring and treatment decisions.

Challenge	Frequency	Percentage
Technical issues with devices	12	92%
Data privacy and security concerns	8	62%
Integration with existing clinical workflows	8	62%
Patient compliance	7	54%
Budget constraints	6	46%
Skin irritation/adverse events	1	8%
Clinical validation of devices	1	8%
AE reporting/related device findings	1	8%

Table 2: Proportion of Experts Flagging Key Implementation Risk

Recommended Use Cases

Most experts (70%) identified cardiovascular disease as the field with the clearest benefit, but neurology (e.g., MS, Parkinson's), respiratory medicine, and musculoskeletal rehabilitation were also noted.

Discussion

The findings from this investigation reinforce the growing evidence for the feasibility and utility of integrating cardiac activity sensors into functional assessments and clinical trial endpoints. In the feasibility pilot, the use of the Apple Watch enabled objective, patient-friendly measurement of multiple outcome metrics with few technical barriers in healthy volunteers. While the sample size was small, all participants completed the digital assessment procedures, suggesting strong compliance potential in appropriately selected clinical populations.

Expert stakeholders confirmed that the main perceived benefits are centred on the reduction of error, additional data granularity, and possibilities for remote, patient-centric study models. These attributes point to a paradigm shift: outcome assessments are no longer discrete, facility-bound events but can transition toward continuous, real-world data streams. Automated digital data capture may thereby support more efficient monitoring, earlier identification of adverse trends, and more personalised patient management.

However, the challenges identified by pharmaceutical industry experts are relevant and centre on operationalisation, risk management, and patient safety:

Device Reliability

An almost universal concern that highlights the need for thorough device validation,

quality control processes, and backup plans for data loss. Close collaboration with device manufacturers and robust SOPs is essential.

Privacy and Ethics

Maintaining data integrity and ensuring robust consent procedures are essential, especially as raw physiological and geolocation data multiply. Regulatory frameworks must catch up to the implications of ubiquitous sensor data.

Workflow Integration

Incorporating digital data flows into regulated clinical trials requires deliberate planning, technical support, and a rethink of standard operating procedures—from data capture through to statistical reporting.

Training and Support

Structured onboarding for both study staff and patients is vital to minimise compliance errors, device misuse, and technical issues.

Clinical Validation

More evidence is needed to confirm that digital measurements are interchangeable or superior to traditional endpoints, and to clarify how to handle discordant results.

It is notable that experts were divided on the degree to which digital sensors improve patient experience, suggesting that engagement strategies need to be tailored and that "*one-size-fits-all*" approaches may not be appropriate, particularly in older or less digitally literate populations.

Limitations

The study is not without limitations. The healthy volunteer pilot was small and lacked a disease comparator group. Industry experts, while representative, may not capture views across broader care settings (e.g., public hospitals, primary care). Nonetheless, the convergent findings across patients and experts support prioritising further research, including controlled trials in clinical populations and health-economic evaluations of digital endpoint deployment.

Conclusions

This research demonstrates that wearable cardiac activity sensors, exemplified by the Apple Watch, can be effectively integrated into the 6-Minute Walk Test for healthy volunteers, with general acceptability and functional data capture. Input from pharmaceutical professionals underscores the substantial potential for improved measurement, data richness, and flexible study designs in clinical trials -balanced

against meaningful operational, regulatory, and ethical challenges.

To realise the promise of digital assessment in trials, stakeholders must address device validation, staff and patient training, data security, and clinical workflow adjustment. Larger studies in patient populations, supported by cross-sector collaboration and clear regulatory guidance, are now warranted.

Recommendations

Device and Data Management

Select validated devices, establish technical support structures, and specify SOPs for malfunction or data loss.

Training

Develop comprehensive training modules for both patients and staff, including troubleshooting guides and clear device usage instructions.

Patient Selection

Consider digital literacy, comorbidities (especially device incompatibilities), and ensure transparent, dynamic consent processes.

Workflow Integration

Foster interoperability between device data streams and trial data management systems; plan for both central and remote oversight.

Ongoing Evaluation

Implement continuous feedback loops to capture user experiences and technical issues, refining protocols iteratively.

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Research Article | Comparing Global Access and Usability of CT Scanners: Radiographers' Experiences in Ireland and Sub-Saharan Africa

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Abstract

Inequitable access to computed tomography (CT) imaging persists across the globe, with profound implications for health outcomes in low-resource settings. This study presents a comparative analysis of CT access and usability, focusing on radiographers' experiences in Ireland (as a high-income, developed context) and Sub-Saharan Africa (SSA; as a low- and middle-income context).

Using a positivist, abductive approach, a semi-structured questionnaire was distributed to CT radiographers in both regions, generating both quantitative and qualitative data on accessibility barriers, usability challenges, and critical user needs. A total of 52 responses (31 from Ireland, 21 from SSA) highlighted both commonalities and stark regional disparities.

Irish radiographers primarily identified workforce and training shortages as major barriers, whereas SSA radiographers emphasised financial, infrastructural, and maintenance challenges. Both cohorts reported issues with CT hardware, particularly table weight and gantry bore limits, but perceived their impact differently.

The study reveals that although radiographers in both contexts express general satisfaction with CT system usability, region-specific priorities and constraints shape their experiences and needs.

The findings emphasise the importance of inclusive, context-sensitive medical device design and regionally tailored strategies to improve CT access, especially in settings where systemic resource constraints outweigh technical interface problems. Strengthening human resources, embracing frugal innovation, and fostering policy reforms are advocated to progress toward equitable healthcare delivery.

Introduction

There is an enduring divide in access to advanced medical imaging, notably computed tomography (CT), between the world's developed and developing regions. CT scanning is integral to the diagnosis, monitoring, and management of a broad range of acute and chronic diseases, providing tangible improvements in patient outcomes and health system efficiency. However, dramatic disparities persist where only 14% of developing countries meet the World Health Organization's (WHO) recommended minimum of one CT scanner per million inhabitants, compared with 100% coverage in developed countries. This "diagnostic divide" is associated with delayed diagnoses, increased morbidity, and significant health inequities, especially in low- and middle-income countries.

The design and deployment of medical devices, such as CT scanners, are often oriented towards the context and requirements of high-resource settings. This approach can exacerbate usability and accessibility challenges in low-resource environments, particularly when contextual and demographic factors are insufficiently considered. Radiographers, as the primary users of CT systems, occupy a critical position in ensuring the safety, effectiveness, and efficiency of imaging services. Yet their voices and experiences are frequently underrepresented in both academic and industry literature, especially in comparative, cross-regional analyses.

This research addresses these interrelated challenges through a comparative user needs assessment of CT radiographers in Ireland and Sub-Saharan Africa (SSA). It aims to 1) document the status of CT access in both regions, 2) examine the user experience and perceived usability of CT scanners, and 3) identify region-specific barriers and critical needs. By situating radiographer perspectives at the centre of the analysis, this study both fills an important gap in the literature and provides actionable insights for policymakers, technology developers, and healthcare institutions committed to delivering equitable imaging services.

Literature Review

The Role of CT in Modern Healthcare

CT imaging has been transformative in clinical diagnostics since its inception, enabling detailed, cross-sectional visualisation of internal anatomy and pathology. Its applications span emergency medicine, oncology, cardiovascular care, trauma management, surgical planning and

interventional radiology. The ability of CT to expedite diagnoses, reduce hospital stays, and enable minimally invasive interventions is well-documented. While alternative imaging modalities such as MRI or ultrasound offer complementary capabilities, CT's speed, versatility, and high diagnostic yield make it a mainstay of contemporary health systems (Khan et al., 2023; Khan & Khan, 2023).

Global Disparities in Access

Despite CT's clinical significance, the global distribution of CT scanners is highly unequal. High-income countries enjoy extensive scanner coverage (on average, more than 20 units per million inhabitants), while most low- and middle-income nations—particularly across SSA—remain severely under-resourced (Nigatu et al., 2023; Frija et al., 2021). Access is further stratified within countries along urban–rural and public–private lines, with rural and low-income populations bearing the greatest burden of underdiagnosis and delayed care (Kawooya et al., 2022; Kiguli-Malwadde et al., 2020).

Barriers to Access and Optimal Use

Barriers to CT access are multifactorial. In high-income settings, issues tend to centre around workforce shortages, procedural backlogs and equipment ageing, while in low-income contexts, financial, infrastructural, and human resource constraints predominate (Hinrichs-Krapels et al., 2023; Aderinto, 2023). Distinctive challenges in SSA include erratic power supply, lack of technical support, insufficient consumables and a reliance on donated, sometimes obsolete or poorly maintained, equipment (Marks et al., 2019; Global Health, 2023). A brain drain of trained radiographers and engineers further compounds these constraints (Ujumadu, 2021).

User Needs and Device Design Biases

Human factors engineering has gained currency within medical device design, emphasising usability, risk mitigation, and the inclusion of diverse user populations (Shaheen et al., 2021). Nevertheless, research and regulatory structures remain biased toward high-income contexts and often exclude minority populations or fail to tailor for resource-poor settings (Congenius, 2023; Davis, 2024). The result, as the WHO and scholars highlight, is that a substantial proportion of medical equipment delivered to developing countries is ill-suited for their environments (Vasan & Friend, 2020).

Radiographer Perspectives: An Evidence Gap

While much usability research on medical devices centres on patient safety or clinician perspectives, systematic data on radiographers' experiences—particularly in cross-context settings—remain sparse (Bitkina et al., 2020; Familoni & Babatunde, 2024). Studies have noted the increasing physical and cognitive workloads for radiographers as CT technology becomes more complex (Aldoihi & Hammami, 2019; Sipos et al., 2024). However, investigations of how these factors intersect with contextual resource constraints, educational background and healthcare systems remain limited.

Conceptual Models for Improved Access

Scholars have recently advanced two dominant models for improving imaging equity: (1) frugal innovation, focused on robust, simplified, cost-effective equipment that prioritises scalability and minimal maintenance for resource-limited settings, and (2) technology leapfrogging, encompassing advanced features such as remote operation, artificial intelligence (AI) assistants, and teleradiology (Ogbole, 2022; Fornell, 2024; Piaggio et al., 2021). Both approaches face challenges related to cost, training, regulatory support, and local adaptation.

The literature thus reveals a tension between technical advancement and contextual appropriateness, with a lack of empirical, radiographer-informed analysis at the heart of the evidence gap.

Methodology

Research Design

This study employed an abductive, positivist research paradigm to gather and interpret empirical data from radiographers in Ireland and SSA. The design integrated structured quantitative inquiry with qualitative, contextual supplementary questions.

Sampling and Data Collection

A semi-structured online questionnaire, developed using Microsoft Forms, was distributed over eight weeks (May–July 2024). Recruitment targeted CT radiographers currently practising in Ireland or SSA via professional networks, social media, and direct contact with healthcare facilities. The questionnaire comprised 30–31 items across four domains: demographics, context of use, user experience, and ranking of needs and priorities. Questions included multiple-choice, Likert-scale, ranking, and optional

open-ended formats. Eligibility required English proficiency and current work in a relevant clinical setting.

Data Analysis

Closed responses were analysed quantitatively, leveraging descriptive statistics and chi-square tests to identify patterns, trends, and associations. Open responses were analysed thematically to extract insights into user experience and contextual differences. Data visualisation tools (bar charts, word clouds) were used to support interpretation. The total sample comprised 31 respondents from Ireland and 21 respondents from six SSA countries (South Africa, Nigeria, Ghana, Rwanda, Lesotho, Zimbabwe).

Ethical Considerations

All participants provided informed consent; no identifying or sensitive data were collected. The study received ethical approval from the relevant institutional review board, and data protection procedures compiled with GDPR standards.

Region	Public Hospitals	Private Facilities	Urban	Rural	Suburban
Ireland	80%	20%	65%	19%	16%
SSA	41%	59%	76%	14%	10%

Table 1: Distribution of Participants by Region and Facility Type

Results

Sample Characteristics

Of 52 respondents, 60% were from Ireland (n=31) and 40% from SSA (n=21). Irish respondents were predominantly female (74%), while SSA respondents were mainly male (57%), reflecting underlying regional education and workforce patterns. The majority in both contexts worked in urban environments; public hospitals dominated in Ireland (80%), whereas private facilities were more common among SSA respondents (59%), mirroring broader healthcare structure

Education, Training, Experience

Most participants (80%) had formal CT education, with master's or postgraduate degrees more common in Ireland; 29% in SSA reported no formal CT-specific education. Manufacturer training and informal peer learning were prevalent in both regions, with manufacturer training more frequent in SSA (62%). Experience varied: 44% had 1–5 years in CT, but SSA respondents skewed towards less experience, likely reflecting higher turnover or brain drain.

CT Scanner Availability And Condition

48% overall had access to only one scanner, with Irish sites more likely to have multiple units (32% had three or more) than SSA (less than 5%). The majority reported their scanners had been acquired as new purchases; only SSA respondents noted reliance on second-hand devices, corroborating existing literature on financial and logistical constraints.

Perceptions of Access Barriers

- In Ireland, the dominant barriers were long waiting lists (55% marked as most significant), staff shortages, and limited training opportunities. Infrastructural issues (e.g., unstable electricity or internet) were negligible. SSA respondents prioritised the high cost (by region)
- In SSA high scanner purchase prices, insufficient technical support, and infrastructural instability. Long waiting lists ranked low, reflecting greater importance given to meeting even baseline demand.

Barrier	Ranked #1 by Ireland (%)	Ranked #1 by SSA (%)
Long waiting lists	55	5
High purchase cost (to facility)	10	34
High cost to patients	0	14
Staff shortage	29	14
Maintenance/technical support	0	19
Infrastructural challenges	0	14
Geographical Obstacles	3	0
Negative perception of healthcare in the community	3	0

Table 2: Top-Ranked Barriers to CT Imaging

Usability and user experience

Radiographers in both contexts generally reported satisfaction with CT system usability. Most felt confident in selecting appropriate protocols, adjust parameters, and perform post-processing tasks with confidence. However, common weaknesses included:

- Table weight limits and gantry bore size: Noted as concerns by respondents in both regions, but these issues were more acute in Ireland owing to the national obesity rate.
- User interface (UI): Most were satisfied, but some Irish respondents noted an excessive number of steps within protocols ("*a lot of clicking*") or occasional confusion, whereas SSA respondents highlighted lags and CT software resilience to unstable connectivity.
- Hardware failures: Scanner malfunctions, particularly in tables and power supply, were frequently cited in both regions—but SSA respondents indicated far lengthier downtimes due to insufficient maintenance and technical support.

Feature	**Ireland**	**SSA**
Image quality	77%	52%
Radiation reduction	61%	33%
Cost effectiveness	19%	48%
Ease of maintenance/support	19%	29%
Advanced imaging capabilities	32%	57%
User-friendly operation	39%	10%
Teleradiology/remote op.	0%	5%
Patient comfort	16%	29%

Table 3: Feature Prioritisation (Proportion Ranking in Top 3.

Ranking of System Priorities

When asked to rank CT system features by importance, Irish radiographers prioritised image quality and radiation reduction capabilities, followed by user-friendly operation and advanced imaging capabilities. SSA radiographers emphasised cost effectiveness, patient comfort and ease of maintenance, as well as image quality and advanced imaging capabilities, with less attention paid to user friendliness or teleradiology.

Responses revealed relatively little interest in teleradiology or remote operation in either setting, even though reporting workload is high in SSA due to radiologist shortages.

Manufacturer Preferences

Siemens Healthineers AG was most frequently identified as the preferred manufacturer due to intuitive UI and reliability, but most respondents with experience across several platforms reported overall competence with all leading brands.

Discussion

The comparative findings affirm both universal and region-specific challenges in CT access and usability. Notably, both Irish and SSA radiographers encounter significant issues with scanner hardware, particularly table weight and gantry size, indicating a global need for more robust designs that can accommodate diverse patient populations and evolving epidemiological trends.

However, the broader context reframes how these similar technical challenges manifest and are prioritised. For Irish radiographers, staff shortages and procedural backlogs are primary bottlenecks, albeit in a context of relative equipment abundance and infrastructural stability. These findings echo national reports that highlight hiring freezes and chronic workforce gaps (Burns, 2024; Cullinane, 2024). Technical enhancements to CT systems—such as improving workflow efficiency or integrating “smart” features—may relieve pressure but cannot substitute for systemic policy and resource interventions.

In contrast, SSA radiographers operate under far tighter constraints: scanner scarcity, costly or unreliable maintenance, frequent infrastructural interruptions, high upfront and downstream costs, and a dominant private sector that limits access for uninsured or rural populations. While usability and UI design matter, they are often overshadowed by existential challenges of equipment availability, cost, and support. Moreover, the relatively low ranking of

radiation safety in SSA's feature prioritisation may reflect a hierarchy of needs, wherein quality and safety can only be prioritised after basic access is secured (Ng'andwe & Bwanga, 2022).

Importantly, both groups demonstrated readiness for technological advancement: SSA radiographers expressed considerable interest in advanced imaging features, despite foundational resource challenges, reinforcing that users in low-resource contexts are not resistant to innovation but require essential infrastructure investments to fully leverage such technologies (Chakravarty, 2022).

This study supports the literature's critique of a "*one size fits all*" approach in medical device development. It highlights the peril of exporting devices un-adapted for the resource profile and organisational realities of target contexts (Vasan & Friend, 2020). Additionally, radiographer perspectives—often undervalued—are shown to be crucial for safe, equitable device deployment

Conclusions

This study elucidates both shared and divergent experiences of CT radiographers in Ireland and Sub-Saharan Africa regarding system access, usability, and operational priorities. While both groups identify hardware and workflow bottlenecks, the gravity and impact of these challenges are shaped by region-specific resource, policy, and infrastructure landscapes. Irish radiographers' needs cluster around workforce and training gaps, while SSA radiographers prioritise cost, maintenance, and infrastructure robustness. Inclusion of radiographer perspectives reveals nuanced usability dynamics and underscores the limitations of device design and deployment strategies that overlook or insufficiently account for local context. Progress towards equitable CT access requires not only improved device design but also structural investment, policy reform, and regionally tailored strategies responsive to on-the-ground user realities.

Recommendations

Device manufacturers should prioritise the development of robust CT scanner hardware, particularly focusing on scan tables and gantries that accommodate a wide variety of patient body types and withstand diverse infrastructural conditions. There is also a pressing need for modular, cost-effective CT systems designed specifically for low-resource settings, emphasising ease of maintenance and straightforward operation—characterised as frugal innovation. Incorporating context-

specific user interfaces, including local language support where possible, is essential for improving user experience and accessibility.

Policymakers and health system leaders are urged to address region-specific needs: in Ireland, efforts should focus on mitigating workforce shortages through strategies for hiring, employee retention, and the expansion of formal training opportunities for CT radiographers; in Sub-Saharan Africa, there must be a dual approach combining investment in both the acquisition of equipment and sustainable local technical capacity-building, as well as the implementation of ongoing maintenance contracts. Further, fostering public-private partnerships is recommended to bridge existing healthcare gaps.

The research community should expand comparative, user-centred investigations across other imaging modalities to build a more holistic understanding of imaging equity. Research should also consider the impact of technical design changes on clinical workflow efficiency and user error rates in varying contexts, while conducting systematic audits of radiographer distribution by modality to support more informed future workforce planning and needs.

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Research Article | A Psychobiotic Diet for the Treatment of Stress, Anxiety & Depression

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Abstract

Depression and anxiety are leading contributors to global disease burden, with up to 30% of individuals showing resistance to standard pharmacological treatments. This review explores the potential of psychobiotic dietary strategies, targeting the microbiota–gut–brain axis (MGBA)—as adjunctive or alternative approaches for managing mental health disorders.

A critical analysis of recent peer-reviewed studies was conducted, focusing on interventions involving psychobiotic diets, probiotic and prebiotic supplementation and fermented food intake. Research examining outcomes in stress, anxiety, and depression was prioritised.

A qualitative narrative synthesis was employed to critically evaluate peer-reviewed clinical and pre-clinical studies exploring psychobiotic dietary interventions and supplementation effects on stress, anxiety and depression.

Evidence indicates that psychobiotic interventions can modulate gut microbiota composition and reduce symptoms of stress, anxiety and depression. Although the number of controlled dietary trials is limited, consistent benefits are reported across supplementation studies, including mood improvement and reduced psychological distress. Effects appear more pronounced when psychobiotics are combined with standard antidepressant therapy. Variability in responses suggest moderating influences such as genetics, baseline mental health, physical activity and dietary adherence.

Psychobiotic dietary approaches demonstrate promising potential in improving emotional wellbeing by modulating the MGBA. However, current evidence is preliminary. Large-scale, long-term, randomised controlled trials are required to establish clinical efficacy, optimal formulations, and personalised applications for psychobiotic interventions in mental health management.

Introduction

The global burden of poor mental health continues to escalate, emphasising the need for effective and sustainable interventions. Anxiety and depression are the most prevalent mood disorders worldwide (Santomauro et al., 2021), with depression affecting over 300 million people and standing as a leading cause of disability (World Health Organization, 2024).

Despite treatment accessibility, up to 30% of individuals remain unresponsive to medication (Zhdanava et al., 2021), prompting a growing interest in complementary strategies drawn from nutritional psychiatry.

The gut microbiome—a dynamic ecosystem of bacteria, viruses, fungi, and protozoa—interacts continuously with the brain via the microbiota–gut–brain axis (MGBA) (Baron, 2013). This bidirectional network operates through neural, hormonal, and immune pathways (Valdes et al., 2018). Diet profoundly influences microbial diversity and composition (Ma et al., 2020; Odiase et al., 2023). Western dietary patterns, high in saturated fats and ultra-processed foods, promote dysbiosis and inflammation, whereas fibre-, polyphenol- and fermented food–rich diets enhance eubiotic balance and mental well-being (Schnorr et al., 2014; Clemente et al., 2015; Obregon-Tito et al., 2015).

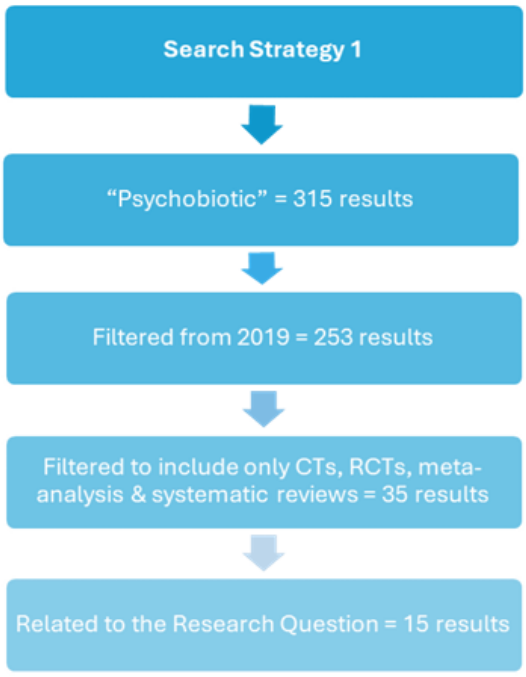
Within this context, the psychobiotic diet, i.e. promoting gut health through prebiotics and fermented foods, emerges as a promising adjunct to conventional mental health therapies (Dinan, Stanton & Cryan, 2013). While supplementation evidence has advanced, research on whole-diet psychobiotic interventions remains limited. This article critically evaluates controlled trials and systematic reviews addressing psychobiotic dietary and supplementation effects on stress, anxiety, and depression, identifying inconsistencies and research gaps.

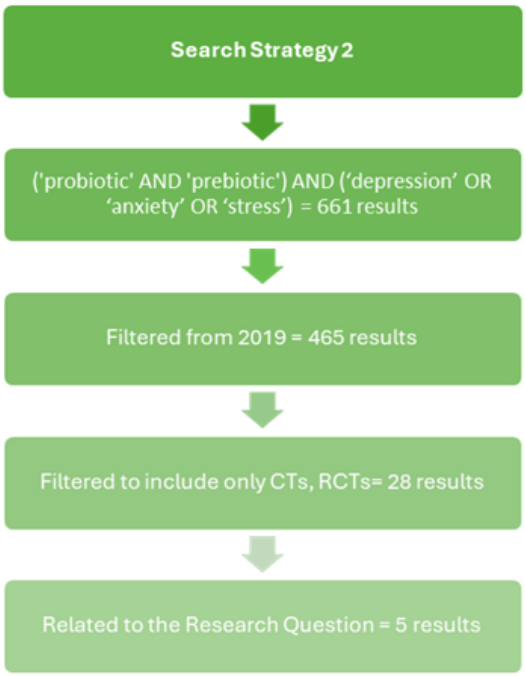
Distinct microbial signatures correlate with mood disorders, notably reduced diversity and depletion of beneficial Bifidobacterium and Lactobacillus in depression (Kelly et al., 2016; Knuesel & Mohajeri, 2021). These bacteria produce short-chain fatty acids (SCFAs) that mitigate neuroinflammation and support blood–brain barrier integrity (Greiner & Bäckhed, 2016; Arora et al., 2021). Mediterranean-style diets mirror psychobiotic principles, fostering microbial richness and improved mood outcomes.

Randomised controlled trials of probiotic strains such as *Lactobacillus plantarum* 299v have demonstrated cognitive and

affective benefits (Rudzki et al., 2019). Symbiotic formulations combining prebiotics and probiotics, including GOS + *Bifidobacterium longum*, have been shown to reduce anxiety under stress (Tian et al., 2022). Although preliminary whole-diet interventions show reductions in stress biomarkers and depressive symptoms (Berding et al., 2023), methodological variability and short durations limit comparability.

Overall, evidence supports the psychobiotic diet's potential to improve mood and reduce stress through microbial modulation. However, long-term efficacy and precise mechanisms remain insufficiently defined. Further multidisciplinary research integrating nutritional science, psychiatry and microbiology is essential to establish robust clinical guidelines for dietary modulation of the MGBA in mental health management.





Methodology

Research Design

The research utilised a qualitative, narrative synthesis methodology to evaluate relevant clinical and pre-clinical studies addressing the psychobiotic diet's effects on mental health.

The literature review followed a structured, multi-phase approach:

Study Selection and Scope

The review incorporated peer-reviewed randomised controlled trials, systematic reviews, and clinical investigations published in English after 2010. The scope included studies examining dietary interventions rich in naturally occurring or supplemented psychobiotic compounds, alongside conventional psychobiotic supplementation trials.

Search Strategy

Database searches were conducted on PubMed, Scopus, and ScienceDirect using Boolean operators combining key terms: "psychobiotic diet", "gut-brain axis", "anxiety", "depression", "prebiotics", "probiotics", and "stress". The search included backward citation tracking and grey literature where appropriate.

Inclusion/Exclusion Criteria

Studies were included if they:

- Involved adult human participants
- Reported on psychological outcomes such as depression, anxiety, mood, or stress
- Applied psychobiotic diets or supplementation for a minimum of two weeks

Exclusion Criteria Involved:

- Non-peer-reviewed publications
- Animal-only studies
- Non-dietary interventions (e.g., faecal transplant)

Data Analysis

Data were thematically coded based on outcome measures, intervention type, participant characteristics and observational duration. The review synthesised findings around three mental health categories: stress, depressive symptoms and anxiety. A separate analysis was conducted to examine results variances and identify methodological constraints.

Results

Findings indicate moderate to strong effectiveness of psychobiotic interventions across all three mental health categories.

Effectiveness of the Psychobiotic Diet in the Treatment of Stress

The best evidence we have for the effectiveness of the psychobiotic diet in the treatment of stress is from a randomised controlled trial conducted by the APC Microbiome Ireland Centre to evaluate the effect of a psychobiotic diet on stress (Berding et al., 2023). The psychobiotic diet consisted primarily of prebiotic-rich fruits and vegetables, grains, legumes and fermented foods. Study participants followed the dietary intervention for 4 weeks (n=45), with outcomes assessed using the Perceived Stress Scale (PSS). There was a statistically significant reduction in perceived stress in the intervention group compared to controls. No significant change in alpha diversity was detected in the bacterial microbiome profile. A separate study assessed the effect of a synbiotic on stress, accounting for participants' physical activity (Quero et al., 2021). Both physically active and sedentary participants received the synbiotic. Both groups experienced

reductions in stress, but the effect was greater in physically active participants.

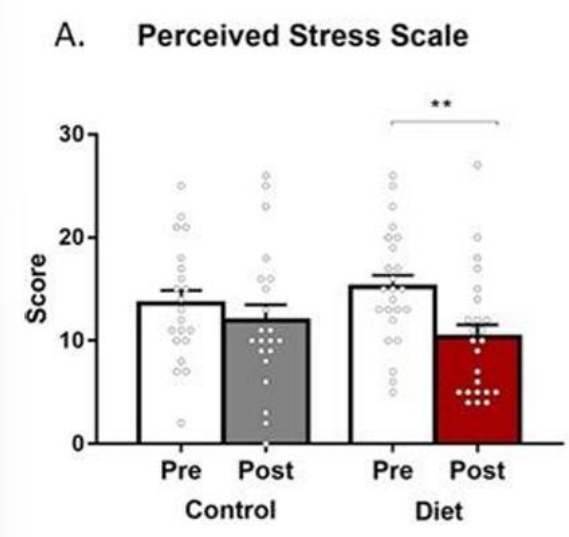


Figure 1: Mean change in PSS scores pre- and post-intervention (Berding et al., 2023).

A further study explored high-prebiotic diets and stress (Mysonhimer et al., 2023). No significant changes in biological stress markers were found between high-prebiotic and control groups, but self-reported well-being improved (Mysonhimer et al., 2023).

Effectiveness of the Psychobiotic Diet in the Treatment of Low Mood/Depression

The "Gut Feelings" Randomised Controlled Trial examined the impact of a psychobiotic diet rich in fibre and fermented foods on individuals with moderate depressive symptoms over six weeks (Freijy et al., 2023). Significant reduction in Montgomery-Asberg Depression Rating Scale (MADRS) scores was found in the intervention group. Additionally, increased intake of fibre, prebiotic foods and fermented foods occurred (Freijy et al., 2023).

Multiple randomised controlled trials reported significant improvements on validated depression scales (e.g., BDI) in groups receiving probiotic interventions versus placebo. *Bifidobacterium breve* CCFM1025 and NVP-1704 studies showed significant improvements in depression scores compared to baseline or placebo (Lee et al., 2021). The "EFFICAD" trial observed significant improvement in BDI with multi-strain supplements (Jackson et al., 2023). Some trials, such as those using 4G-beta-D-Galactosylsucrose or the "IBMA" trial, did not observe a significant effect (Tarutani et al., 2022).

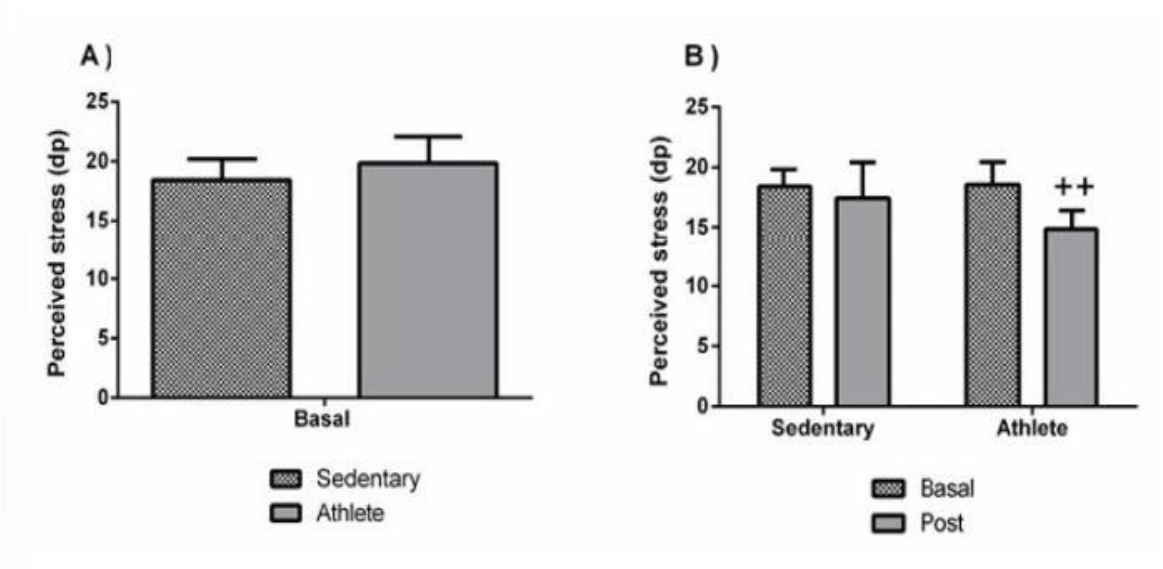
Effectiveness in the Treatment of Clinical Anxiety Disorders

A randomised controlled trial tested the addition of a multispecies probiotic formula to standard therapy in Generalised Anxiety Disorder (GAD) (Eskandarzadeh et al., 2021). Improved STAI scores occurred in the probiotic group versus standard therapy alone. With respect to the effectiveness of

psychobiotics in reducing sub-clinical anxiety, a study identified that carriers of the allele of the IL-1β gene receiving a multi-strain psychobiotic had greater reduction in anxiety compared to non-carriers, with benefit in both (Hall et al., 2004; Karki et al., 2015). In a study involving college learners, *Lactobacillus plantarum* JYLP-326 improved anxiety, depression and insomnia (Zhu et al., 2023). *Lactobacillus gasseri* CP2305 improved depression, anxiety, and sleep in young adults under chronic stress (Zhu et al., 2023). HK-PS23 supplementation reduced depression and anxiety in nurses (Wu et al., 2022). The "Gut-Brain" study reported reduced tension and improved well-being in adults with probiotic supplementation (Tran et al., 2019).

Synopsis of Major Findings

- The psychobiotic diet can reduce perceived stress.
- Psychobiotic supplementation is effective for improving stress, depression, and anxiety.
- Effects are evident in healthy, sub-clinical, and clinical populations across both food-based and supplement-based interventions, though the magnitude and consistency vary.



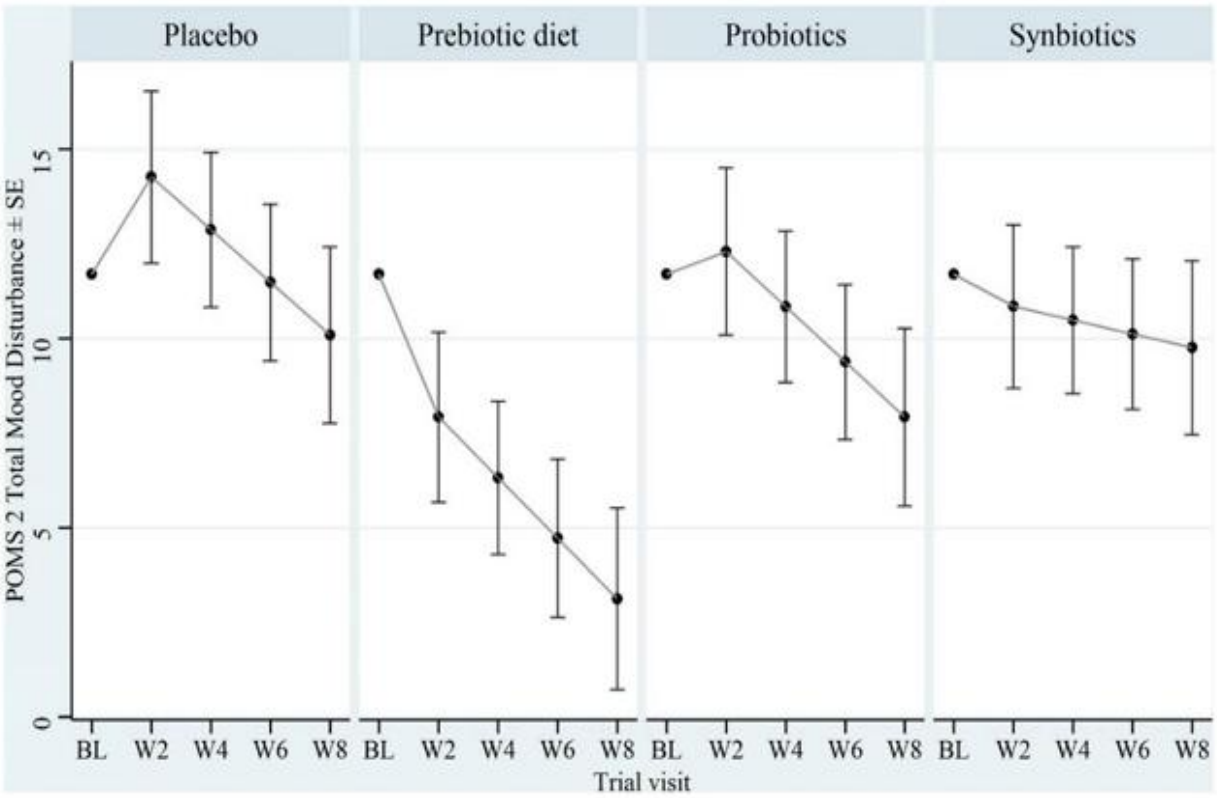


Figure 2: Differences in stress reduction by exercise category following synbiotic administration (Quero et al., 2021)

Discussion

The findings from recent literature make it clear that psychobiotics, whether administered as either diets or supplements, can have a positive impact on stress, depression, and anxiety. In studies assessing stress reduction, interventions featuring a psychobiotic diet or supplementation with probiotics, prebiotics, or synbiotics resulted in lower stress or perceived stress levels among participants.

Specifically, the APC Microbiome Ireland trial and several supplementation studies revealed reduced stress scores in groups receiving such interventions. Reductions in stress were most pronounced in individuals who maintained a higher level of physical activity, as seen in the synbiotic intervention study, which reported greater effects for active participants. However, some contrasting evidence was presented by the University of Illinois, where a trial using a high-prebiotic diet did not show a significant change in biological stress indicators, even though participants in the intervention group described improved subjective well-being.

Regarding depression, the evidence is similarly encouraging. The "*Gut Feelings*" randomised controlled trial demonstrated a significant reduction in depressive symptoms for participants adhering to a psychobiotic diet. In addition to this, numerous randomised controlled trials and clinical studies employing both probiotic and prebiotic supplements—such as those using combinations of Bifidobacterium and Lactobacillus strains, as well as the NVP-1704 psychobiotic—reported notable improvements over placebo groups or baseline symptoms. Studies in patients with major depressive disorder also indicated enhanced outcomes following psychobiotic supplementation, while the EFFICAD trial observed a marked improvement in Beck Depression Inventory scores where a multi-strain probiotic was used. Nevertheless, not all studies found significant effects. For example, randomised controlled trials involving 4G-beta-D-Galactosylsucrose or those from the IBMA clinical trial did not register significant advantages for psychobiotic intervention. Despite these mixed results, meta-analyses and systematic reviews confirmed that psychobiotic supplementation is associated with moderate improvements in depressive symptoms, with trials of longer durations generally reporting the strongest outcomes.

Anxiety disorders and sub-clinical anxiety have also been extensively studied in this context. Multiple studies incorporated multispecies probiotic strategies as adjuncts in the management of generalised

anxiety disorder and saw improved anxiety scores relative to standard therapy alone. Further, certain genetic backgrounds, such as carriers of the A allele of the interleukin-1 beta gene, appeared to derive even more substantial reductions in anxiety from psychobiotic supplementation. Across a spectrum of healthy, stressed, and clinical participants—including learners undergoing examination stress, young adults exposed to chronic stress, and nurses—a consistent pattern emerged: supplementation with specific bacterial strains (such as Lactobacillus plantarum, Lactobacillus gasseri, and HK-PS23) improved symptoms of anxiety, depression, sleep disturbance, and overall psychological well-being.

Despite these promising results across various populations and endpoints, the literature reveals several important limitations. Most studies exploring psychobiotic diets are relatively brief and feature small sample sizes; longer-term impacts and sustained dietary adherence have yet to be thoroughly examined. In addition, the majority of research to date has centred on supplementation rather than comprehensive, food-based or whole-diet interventions. The evidence base would benefit from more large-scale, randomised controlled studies that directly compare the effects of supplement use and dietary patterns rich in prebiotic and probiotic foods. The current findings support a role for psychobiotics as effective adjuncts to traditional treatment for stress, depression, and anxiety. However, the need for future research, including better defined dietary intervention protocols, broader participant samples, and more extended follow-up, remains urgent for providing more conclusive guidance for clinical and public health practice.

Conclusions

The evidence demonstrates that both psychobiotic dietary interventions and psychobiotic supplements can play a beneficial role in reducing stress and alleviating the symptoms of depression and anxiety. Among the interventions studied to date, the greatest and most consistent support is found for psychobiotic supplementation, particularly those involving specific probiotic or synbiotic formulations. However, the psychobiotic diet itself shows promising potential, especially where it emphasises a sustained increase in the consumption of prebiotic- and probiotic-rich foods while minimising the intake of ultra-processed and unhealthy dietary components. It is also evident that the magnitude and consistency of these effects can vary considerably depending on

the nature of the intervention, the duration over which it is applied, individual participant characteristics and the robustness of the underlying study design. Variations in baseline mental health, physical activity, genetic background, and adherence all appear to play notable roles in influencing how individuals respond to psychobiotic strategies. While the existing evidence base is encouraging, it nonetheless highlights the need for more rigorous, extensive, and high-quality research to fully clarify the effectiveness of both supplementation and whole-diet interventions, and to guide their practical application within clinical and public health contexts.

Moving forward, it is recommended that research efforts focus on defining and standardising the essential components of the psychobiotic diet to facilitate comparison across studies and to support future dietary guidelines. There should be a particular emphasis on prioritising long-term, food-based interventions, rather than relying predominantly on short-term supplementation, to more accurately assess the sustained benefits and real-world practicality of psychobiotic dietary changes. A deeper investigation into gene–diet interactions is warranted, as individual genetic make-up may account for variations in response and could eventually allow for more personalised and effective dietary recommendations. Lastly, as the body of evidence grows, it will be increasingly important to develop public health and clinical guidelines that integrate the psychobiotic diet and supplementation strategies, ensuring that emerging knowledge is translated into accessible, evidence-based advice for practitioners and the wider community.

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