2025 Science & Research Updates

PANEL

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MATT HALMA

MODERATED BY

DR.
JOSEPH VARON

IMA's Four Pillars

- Combating Chronic Disease
- Patient Empowerment
- Transparency in Medicine
- Building a Healthy Culture

SCIENCE

Science is a systematic way of understanding the natural world through observation, experimentation, and reasoning.

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Science and Publications

- **Science:**
  - Involves observation, experimentation, and analysis.
  - Generates data and insights.
  - Aims to answer specific questions or test hypotheses

- **Publications:**
  - Are the formal record of **scientific findings**
  - Include things like original research articles, reviews, case reports, and letters
  - Follow a standard structure (e.g., Introduction, Methods, Results, Discussion—aka **IMRaD**)
  - Go through **peer review** to ensure quality and credibility
  - Are **published** in journals (e.g., *Nature*, *The Lancet*, *JAMA*, etc.)

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Journal of INDEPENDENT MEDICINE™

JournalOfIndependentMedicine.org

- Peer-Reviewed
- Transparency
- Underreported Topics
- No Big Pharma Influence

Joseph Varon, MD, FACP, FCCP, FCCM, FRSM
Editor-in-Chief
President and Chief Medical Officer, Independent Medical Alliance

INDEPENDENT™ MEDICAL ALLIANCE

Goals

- This journal will be a sanctuary for researchers and clinicians who want to engage in Honest Medicine and publish findings that can truly help patients, rather than serve financial interests

- Our goal is *simple but profound*—restore trust in medical research by publishing truthful, high-quality science that is free from corporate and political influence

Journal
of INDEPENDENT MEDICINE

In memoriam

Journal of Independent Medicine

A Doctor's Lasting Echo: The Unspoken Cry for Help

Katarina Lindley[1]

In the hallowed halls of medicine, where life and death dance a delicate cotillion, there exists a shadow seldom spoken of the suicide of doctors. This essay is not a statistical analysis or a call to action; it's a lament, a heartfelt reflection on the lives of those who, paradoxically, save lives while silently suffering.

Doctors, often perceived as invincible heroes, are in reality, just as vulnerable as the patients they care for. The relentless pursuit of perfection in the medical profession leaves little room for personal struggles. This is where the story unfolds, in the silent corners of a physician's mind where despair can take root.

The narrative of a doctor's suicide is woven with threads of pressure, burnout, and isolation. The pressure to perform, to never err, is a silent killer. Each mistake, each patient lost, becomes a scar, not just on the record but on the soul. Burnout, a clinically discussed term, is, in reality, a smoldering fire that consumes slowly but surely. And isolation? In a field where empathy is taught but often self-care is neglected, loneliness becomes the doctor's unwanted companion.

Consider the story of a young resident, brilliant yet overwhelmed by the system's expectations. The sleepless nights, the endless shifts, the constant fear of missing something critical. His suicide was a shock, but for those who knew him intimately, it was the culmination of a battle fought in silence. His note, if there was one, might have echoed the sentiment, "The things that make me happy no longer outweigh the things that make me sad."

Then there's the story of a seasoned surgeon whose hands have saved countless lives but could not save her from her despair. Her colleagues might speak of her brilliance, her patients of her kindness, but none knew the depth of her solitude or the weight of her unspoken burdens. Her loss left a void, not just in the medical community but in the hearts of those who knew her as more than a doctor.

While unique in their details, these stories share a common tragedy: the inability to reach out and admit vulnerability. The medical culture, which prides itself on resilience, often misses the mark when it comes to mental health. Doctors are expected to heal, but who heals the healer when the healer is broken?

This essay is a call to action, a plea for change. For every doctor who has felt the weight of their profession, for every life lost to this silent epidemic, change is imperative. We must create an environment where mental health is as routinely checked as physical health, where seeking help is a sign of strength, and where the healing of the healer is as important as the healing of the patient.

To all those in the medical profession, remember that your worth is not solely measured by the lives you save, but also by the life you lead. It's okay to be vulnerable, to reach out, and to seek help. Your story doesn't have to end in tragedy; it can be a testament to the resilience that is possible in both medicine and life.

On a personal note…

We have recently lost one of our own. A wonderful soul, a fearless warrior, a lioness defender of the truth, and a gentle mother who wiped many of our tears. Many of us are asking ourselves if we have failed her. How did we miss her cries? What could we have done? I don't have the answer to those questions yet, but I find peace in knowing that she is watching us from above. We may have lost the earthly star, but we have gained a heavenly one that is shining the light for us here on Earth. I still hear her laughter and her words encouraging me to go on. Her spirit will continue guiding me and others, and her light will shine bright for future generations.

In memoriam, **Dr. Jackie Stone,** FLCCC Senior Fellow, Holistic and Integrative Medicine (1965-2024).

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Original article

Journal of Independent Medicine

Integrative Analysis of Neutrophil to Lymphocyte Ratio, CD4+, and CD8+ Cell Counts in COVID-19 Patients: A Retrospective Cohort Study

Claudia M. Ramirez[1], *Mohamed Ziad-M. Said*[2,3], *Andreu Comas-Garcia*[4], *Pedro Carmo*[1], *Jesus Mendez-Castro*[1], *Joseph Varon*[1,3,5,6]

Abstract

Introduction: **Immune dysregulation affecting neutrophils, CD4+, and CD8+ T lymphocytes is common in severe coronavirus disease 2019 (COVID-19) cases. This study assessed the association between neutrophil-lymphocyte ratio (NLR), CD4+ and CD8+ counts, and outcomes in COVID-19 patients.**

Methods: **A retrospective study on adult patients admitted to a COVID-19 critical care unit between March 2020 and February 2022. Admission, leukocytes, and lymphocytes were obtained, and NLR was calculated. Also, CD4+ and CD8+ cell counts were recorded upon hospital admission and at their lowest point during the hospitalization. A receiver operating characteristic (ROC) curve was used to predict mortality risk and determine the best cutoff values for NLR, CD4+, and CD8+. Based on these cutoffs, the patients were divided into groups and then analyzed based on demographic characteristics, severity scores, and laboratory findings, which were compared between the groups. Primary outcomes were the length of stay (LOS), the need for cardiopulmonary resuscitation (CPR), and survival at hospital discharge. Descriptive statistics, Mann-Whitney U, Chi², Fisher exact tests, multivariate analysis, bivariate analysis, and multiple linear regression were utilized.**

Results: **For NLR analysis, 985 patients were included. The odds ratio (OR) of death for patients with NLR ≥3.63 on admission was 3.53 (2.51-4.98); p<0.001. The adjusted OR (aOR) of death for these patients was 1.5 (1.003- 2.436); p=0.049. 439 patients (44.5%) had NLR ≥3.63, while 546 patients had NLR<3.63 (55.4%). It was observed that patients with an NLR value of ≥3.63 were more commonly older than 65 years (72%), male (64.7%), and of Caucasian race (24.9%) compared to those with an NLR<3.36; p<0.001. To analyze CD4+ cells, 798 patients with available CD4+ cell counts at hospital admission were included. ROC logistic regression found that a <200 cells/µl count was associated with an increased risk of death. Of these patients, 583 (73.1%) had ≥200 CD4+ T cells/µl, and 215 (26.9%) had <200 CD4+ T cells/µl. Acute Physiology and Chronic Health Evaluation II (APACHE II), sequential organ failure assessment (SOFA), and ICHIKADO CT scores on admission were all higher in the group with lower CD4+ cell counts.**

This group also had a higher rate of CPR need (21.9% vs. 11.0%, p<0.001), LOS (8 days vs. 7 days, p=0.049), and higher mortality (34.0% vs. 15.1%, p<0.001) when compared to higher CD4+ cell counts. For the analysis of CD8+ cells, 797 patients with available CD8+ cell counts at admission were included; ROC logistic regression found that a <100 cells/µl count was associated with an increased risk of death. Of these patients, 628 (78.8%) had ≥100 CD8+ cells/µl, and 167 (21.2%) had <100 CD8+ cells/µl. The group with lower CD8+ cell counts had higher APACHE II, SOFA, and ICHIKADO CT scores, as well as prolonged LOS (9 days vs. 7 days, p<0.001), higher rates of CPR (23.3% vs. 10.5% p<0.001), and higher mortality (41.3% vs. 14.5% p<0.001) when compared with higher CD8+ cell counts.

Conclusions: **Admission NLR ≥3.63, CD4+ <200 cells/µl, and CD8+<100 cells/µl were associated with worse outcomes. CD8+<100 cells/µl, along with patient characteristics and biochemical markers, appears to be a stronger predictor of the need for CPR, prolonged LOS, and in-hospital mortality. Additionally, a significant drop in CD4+ or CD8+ levels during hospitalization was a strong indicator of in-hospital mortality.**

Keywords: COVID-19, lymphocytes, $CD4^+$, $CD8^+$, in-hospital mortality, severe acute respiratory syndrome.

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Review

Journal of Independent Medicine

Traditional Chinese medicine (TCM) - A review (part 1)

Pei Harris[1], *Adylle Varon*[2]

Abstract

Having been used for over 5,000 years in Asian countries, traditional Chinese medicine (TCM) has emerged as a highly sought-after alternative treatment option both during and after the COVID-19 pandemic. This article provides an overview of TCM, covering its history and roots in culture and philosophy, core concepts and theories, definitions of terms used in TCM, and examples of TCM being used in clinical settings. Both traditional Chinese and English versions of the titles of each TCM publication, along with the names of TCM theories, modalities, and key concepts, are provided.

This review is divided into two sections and has five components overall. Part 1 includes the following elements: the summary, the history of TCM, core concepts and theories of TCM, and definitions of acupuncture, moxibustion, and acupressure; part 2 includes the summary, definitions of the rest of TCM modalities and TCM clinical application examples. This is the part 1 of the review.

Keywords: Traditional Chinese medicine (TCM), acupuncture, acupressure, long-COVID, neurological disorders, qi.

History of TCM

Traditional Chinese Medicine (TCM) is rooted within Chinese culture, and it was founded at least five thousand years ago on the Central Plain of the Yellow River Basin in northern China. (1) The first medical literature on herbal medicine were discovered in Classic of Changes 易經 (Yi Jing) and Classic of Poetry 詩經 (Shi Jing). (1-4) Later, TCM evolved into a separate discipline as acquired knowledge was chronicled in medical publications. (2-4) The most well-known and fundamental four classics include the Inner Canon of the Yellow Emperor 黃帝內經 (Huang Di Nei Jing, ~26 BCE), Yellow Emperor's Canon of Eighty-One Difficult Issues 黃帝八十一難經 (Nan Jing, ~106 CE), Treatise on Cold Damage Disorders 傷寒論 (Shang Han Lun, ~206 CE), and Shennong's Materia Medica 神農本草經 (Shen Nong Ben Cao Jing, ~220 CE). (2-4)

Prior to the sixth century AD, Chinese Buddhist priests introduced Chinese medicine to Korea and Japan. During the Tang period (618–907), traveling priests further disseminated Chinese medical expertise to these regions. (3)

According to World Health Organization (WHO) statistics, TCM has been recognized by 29 nations and territories, including Australia, Canada, Austria, Singapore, and Vietnam, through legislation, with 18 countries and regions covering Traditional Chinese Herbal Medicine (TCHM) in medical insurance. Many TCHMs have been registered sequentially in the European Union (EU), Russia, Singapore, Cuba, and Vietnam. In contrast to the EU and other nations, TCHM must submit a new drug application (NDA) for marketing in the United States. This is in accordance with the FDA's Guid-

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Repurposed drugs

Journal of Independent Medicine

Ivermectin, a Molecular Swiss Army Knife: A Review of Mechanisms, Indications and Safety Concerns in Drug Repurposing

Matthew Halma[1], *Paola Vottero*[2]

Abstract

Ivermectin, originally developed for the treatment of parasitic diseases such as onchocerciasis (river blindness), has earned its title of "wonder drug" due to its broad-spectrum therapeutic activity. Ivermectin's potential to address unmet global health challenges makes it an important focus for future medical research. This review explores ivermectin's mechanisms of action and its expanding therapeutic applications, including in parasitic, bacterial and viral infections, and cancer among other disorders. It demonstrates a robust safety profile, and wide scale studies have found a low rate of adverse events. This review highlights the ongoing research and emphasizes the need for careful consideration of both the benefits and risks of ivermectin. Further studies are required to support its repurposing for new indications.

Introduction

The discovery of ivermectin was serendipitous and fortuitous, it is a story in which the discovery could have easily been missed, and billions of people deprived of its benefits. Ivermectin's illustrious story begins in 1972, when Dr. Satoshi Ōmura launched a research project to bioprospect for antibiotics from organisms in natural environments (**Figure 1**). (1) Ōmura of the Kitasato Institute in Japan formed a collaboration the next year with the laboratories of Merck, Sharpe and Dohme (MSD) in the United States, led by Dr. William Campbell.

Between 1973 and 1974, Ōmura collected soil samples to screen for the biological activity of compounds. One of these samples, collected at a golf course in Kawana, about 80 miles outside Tokyo, was sent to the MSD laboratories for testing as an antihelminthic agent. (2) Sample number MA-4680 showed potent anthelmintic activity across a broad range of concentrations, with crude extracts potently inhibiting roundworms at concentrations as low as 0.0003%. (3) The compound appeared safe, as the toxicity observed in the *in vivo* tests was attributable to a microbial metabolite, which could be removed in subsequent isolation. (3) The anthelminthic compound was named avermectin, and the bacterial species which produced it was named *Streptomyces avermitilis*. The discovery of *Streptomyces avermitilis by* Ōmura was extremely fortunate, it wasn't until 1992 that another isolate of the same species was found in a field sample in Italy. (4) Since then, the bacterium has been discovered only a handful more times from soil samples, underscoring its rarity. (5,6)

Ivermectin (IVM) has been widely used throughout

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Ending

~~Tackling~~ Chronic Disease Burden

A research roadmap

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Top sources of disease burden in the USA (2022)

Burden of disease scenarios by state in the USA, 2022–50: a forecasting analysis for the Global Burden of Disease Study 2021
Mokdad, Ali H et al. The Lancet, Volume 404, Issue 10469, 2341 - 2370

2022 Leading causes	Age-standardised rate (per 100,000)
1 Drug use disorders	1965·7 (1662·4 to 2267·1)
2 Ischaemic heart disease	1491·9 (1383·6 to 1567·9)
3 COVID-19	1242·9 (1009·3 to 1594·6)
4 Low back pain	1180·6 (858·0 to 1536·9)
5 Other musculoskeletal disorders	976·4 (704·4 to 1293·7)
6 Diabetes mellitus	960·7 (764·8 to 1198·8)
7 Depressive disorders	799·1 (566·9 to 1084·4)
8 Chronic obstructive pulmonary disease	776·2 (725·6 to 820·7)
9 Road injuries	710·6 (653·2 to 769·3)
10 Stroke	689·1 (627·3 to 747·3)
11 Headache disorders	686·2 (136·8 to 1451·0)
12 Neonatal disorders	684·4 (609·7 to 766·3)
13 Anxiety disorders	660·3 (460·7 to 891·5)
14 Self-harm	639·0 (615·9 to 660·0)
15 Tracheal, bronchus, and lung cancer	624·4 (587·1 to 649·9)
16 Alzheimer's disease and other dementias	520·6 (240·1 to 1089·2)
17 Falls	468·9 (372·8 to 591·5)
18 Chronic kidney disease	421·4 (389·0 to 443·4)
19 Age-related and other hearing loss	420·2 (294·8 to 583·4)
20 Asthma	418·0 (283·9 to 611·3)

Our Approach

- Identify natural products and repurposed drugs for chronic diseases with the highest evidentiary basis
- Validate
- Iterate
- Connect Basic Science with Clinical Application

Our Targets

- Opioid Use Disorder (OUD)
- Chronic Pain
- Spike protein related diseases
- Depression
- Dementia
- Nervous System disorders (anxiety, autism)
- Hypertension
- Hypothyroidism
- Diseases of Aging

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Why?

- After decades of the same approach, chronic disease is still high, in many cases rising still.
- Aging trends mean an increased level of chronic age-related diseases - early intervention averts disaster
- Repurposed drugs and natural products obviate issue of drug shortages

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2022 Leading causes	Age-standardised rate (per 100,000)	
1 Drug use disorders	1965·7 (1662·4 to 2267·1)	W
2 Ischaemic heart disease	1491·9 (1383·6 to 1567·9)	
3 COVID-19	1242·9 (1009·3 to 1594·6)	
4 Low back pain	1180·6 (858·0 to 1536·9)	W
5 Other musculoskeletal disorders	976·4 (704·4 to 1293·7)	✔
6 Diabetes mellitus	960·7 (764·8 to 1198·8)	✔
7 Depressive disorders	799·1 (566·9 to 1084·4)	✔
8 Chronic obstructive pulmonary disease	776·2 (725·6 to 820·7)	W
9 Road injuries	710·6 (653·2 to 769·3)	
10 Stroke	689·1 (627·3 to 747·3)	
11 Headache disorders	686·2 (136·8 to 1451·0)	W
12 Neonatal disorders	684·4 (609·7 to 766·3)	
13 Anxiety disorders	660·3 (460·7 to 891·5)	W
14 Self-harm	639·0 (615·9 to 660·0)	
15 Tracheal, bronchus, and lung cancer	624·4 (587·1 to 649·9)	✔
16 Alzheimer's disease and other dementias	520·6 (240·1 to 1089·2)	✔
17 Falls	468·9 (372·8 to 591·5)	
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20 Asthma	418·0 (283·9 to 611·3)	

W: Work in progress
: Published work

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Contents lists available at ScienceDirect

Brain Behavior and Immunity Integrative

journal homepage: www.editorialmanager.com/bbii

Lifestyle medicine for healthy cognitive aging: A narrative review

Matthew Halma [a,*], Paul Marik [b], Suzanne Gazda [c], Jack Tuszynski [d,e,f]

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nutrients

Review

Cancer Metabolism as a Therapeutic Target and Review of Interventions

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pharmacoepidemiology

Article

DARE-SAFE: Denominator-Adjusted Rate Estimates of Substance Adverse Events Frequency Evaluation in Pharmaceuticals and Vaccines

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Contents lists available at ScienceDirect

Endocrine and Metabolic Science

journal homepage: www.elsevier.com/locate/endmts

Review

Exploring autophagy in treating SARS-CoV-2 spike protein-related pathology

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Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics Plus

journal homepage: www.sciencedirect.com/journal/archives-of-gerontology-and-geriatrics-plus

Blood biomarkers associated with all-cause mortality risk: Accessibility and clinical utility for lifestyle medicine

Matthew Halma [a,b,*], Mariyam Aniwar [c], Edgar Selem [d], Jack Tuszynski [e], Joseph Varon [b], Paul Marik [b]

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frontiers | Frontiers in Chemistry

Therapeutic potential of compounds targeting SARS-CoV-2 helicase

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Journal of American Physicians and Surgeons

AAPS

Potential Dietary and Lifestyle Interventions for Decreasing Insulin Resistance

psychology international

Review

Integrative Interventions for Improving Outcomes in Depression: A Narrative Review

Matthew Halma [1,*], Christof Plothe [1] and Paul E. Marik [2,*]

Review

INFECTIOUS DISEASES & IMMUNITY

OPEN

Alterations of SARS-CoV-2 Evolutionary Dynamics by Pharmaceutical Factors

Matthew Halma*

EbMCsquared CIC, Bath BA2 4BL, United Kingdom.

DE GRUYTER

Open Health 2024; 5: 20230

Matthew Halma*

Towards robust pharmacovigilance surveillance systems

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microorganisms

Review

Strategies for the Management of Spike Protein-Related Pathology

Matthew T. J. Halma [1], Christof Plothe [2], Paul Marik [3] and Theresa A. Lawrie [1,*]

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Journal of Functional Morphology and Kinesiology

MDPI

Review

Reversing Decline in Aging Muscles: Expected Trends, Impacts and Remedies

Matthew Halma [1,2], Paul Marik [2], Joseph Varon [2] and Jack Tuszynski [1,3,4,*]

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Multidisciplinary Scientific Journal

The Novelty of mRNA Viral Vaccines and Potential Harms: A Scoping Review

Matthew TJ. Halma, Jessica Rose, Theresa Lawrie

Refocusing the NIH

Paul E. Marik, MD, FCCM, FCCP

Questions

- Does Vitamin D prevent and improve outcome of cancer?
- Does ivermectin have a role in the treatment of cancer?
- Does ivermectin have a role in the treatment of type II diabetes?

Global Importance, Global Impact…

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The Journal of Clinical Endocrinology & Metabolism, 2024, **00**, 1–41
https://doi.org/10.1210/clinem/dgae290
Advance access publication 3 June 2024

Clinical Practice Guideline

Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

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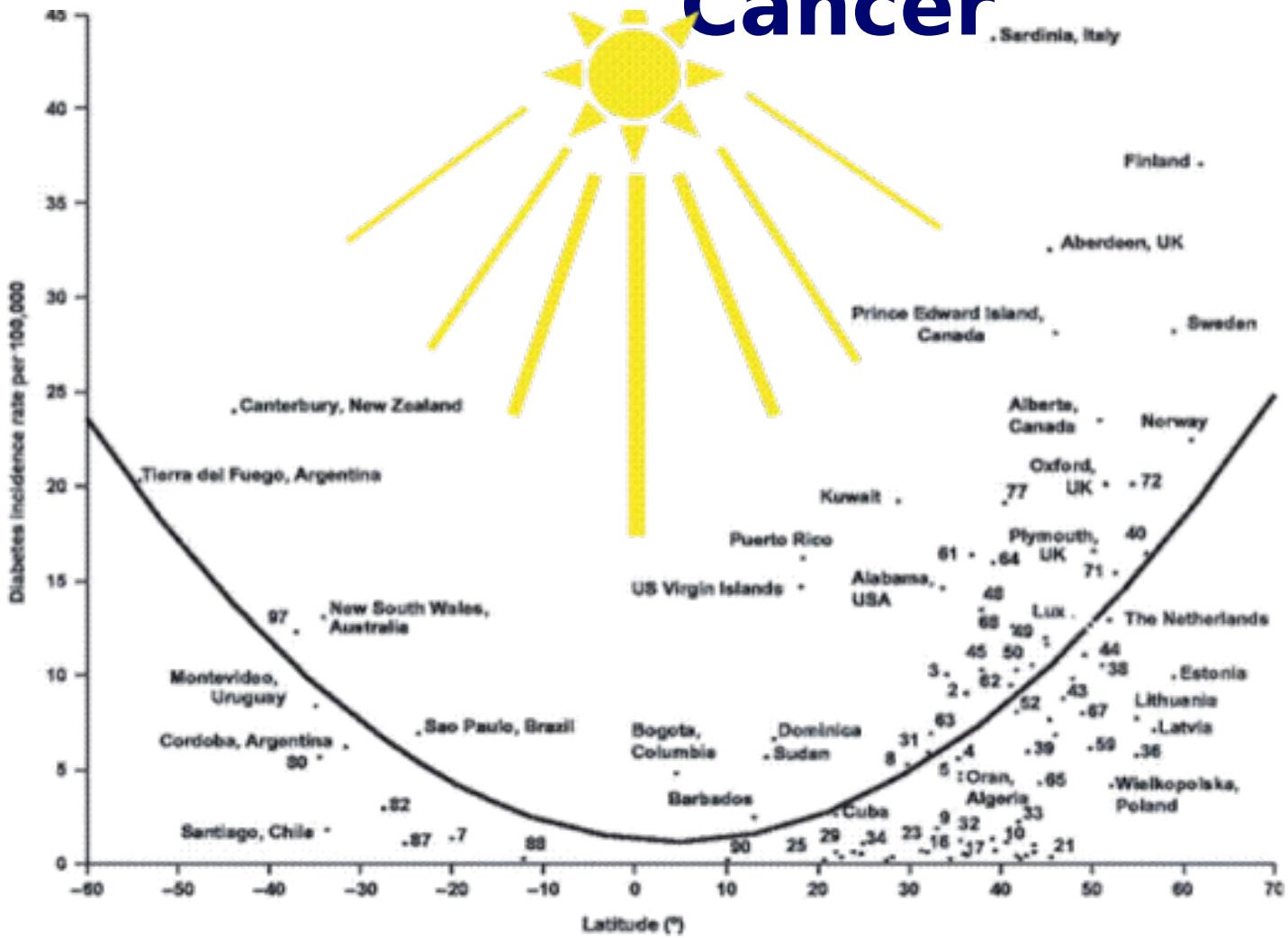
Vitamin D, Latitude and Risk of Cancer



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BJC British Journal of Cancer

www.nature.com/bjc

ARTICLE

Epidemiology

The effect of vitamin D supplementation on survival in patients with colorectal cancer: systematic review and meta-analysis of randomised controlled trials

Peter G. Vaughan-Shaw[1,2], Louis F. Buijs[1,2], James P. Blackmur[1,2], Evi Theodoratou[2,3], Lina Zgaga[4], Farhat V. N. Din[1,2], Susan M. Farrington[1,2] and Malcolm G. Dunlop[1,2]

CONCLUSIONS: Meta-analysis demonstrates a clinically meaningful benefit of vitamin D supplementation on CRC survival outcomes.

British Journal of Cancer (2020) 123:1705–1712

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AI Ranking Top 5 Anti-Cancer Drugs

Combining anti-cancer ranking, Stem Cell pathway activity and safety.

Rank	Compound	Pathways Targeted	Safety Category
1	Ivermectin	WNT, Notch, Hedgehog	Safe
2	Mebendazole	WNT, Hedgehog	Safe
3	Fenbendazole	WNT, Hedgehog	Safe
4	Curcumin	All except JAK/STAT	Safe
5	Resveratrol	WNT, Notch	Safe

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nature COMMUNICATIONS

ARTICLE

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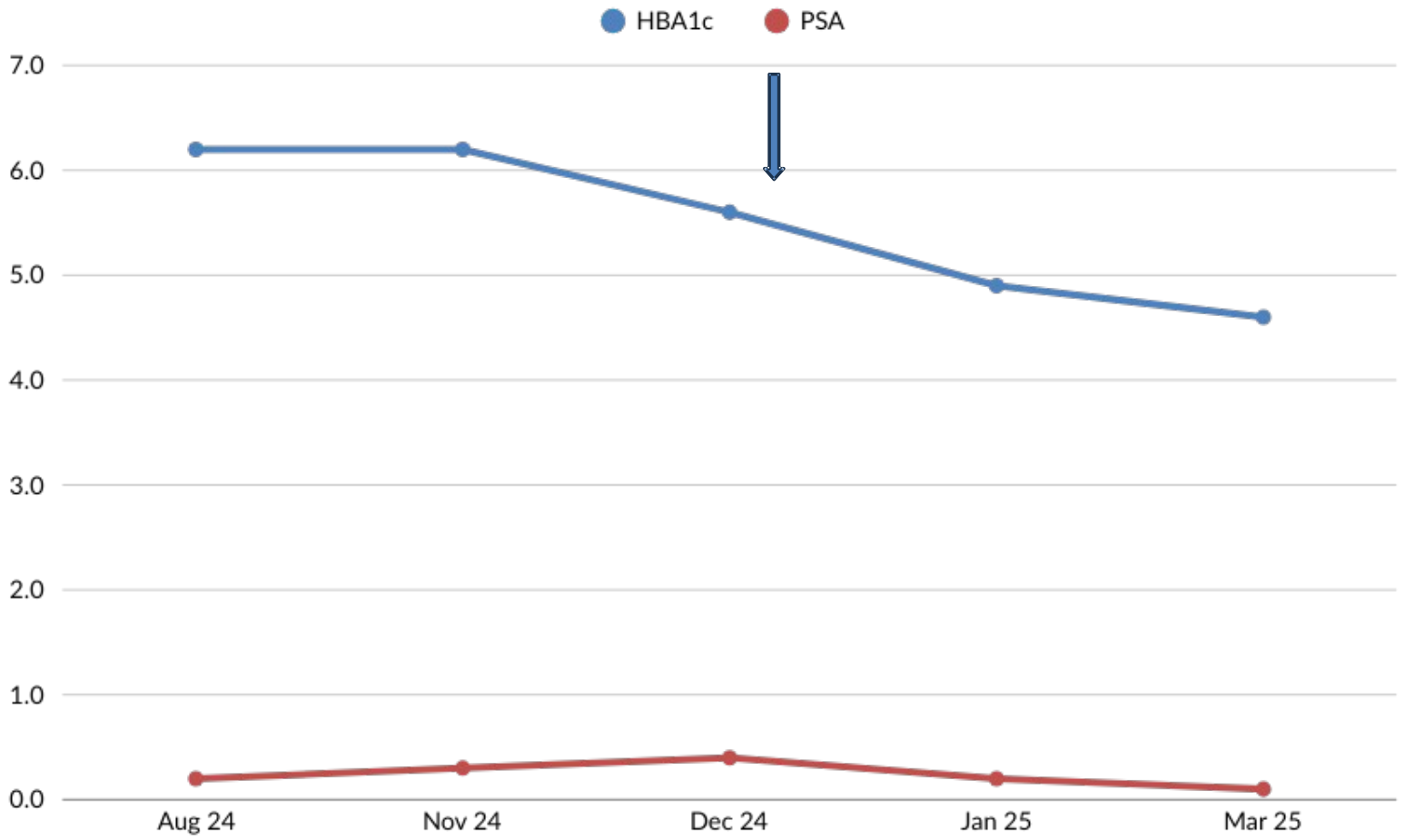
The antiparasitic drug ivermectin is a novel FXR ligand that regulates metabolism

Lihua Jin[1,*], Xuhui Feng[1,*], Hui Rong[2], Zhifu Pan[1], Yuka Inaba[2], Lin Qiu[1], Weili Zheng[1], Shengchen Lin[1], Rui Wang[1], Zhao Wang[1], Shanshan Wang[1], Hongyan Liu[1], Song Li[2], Wen Xie[2] & Yong Li[1]

Magic Drug



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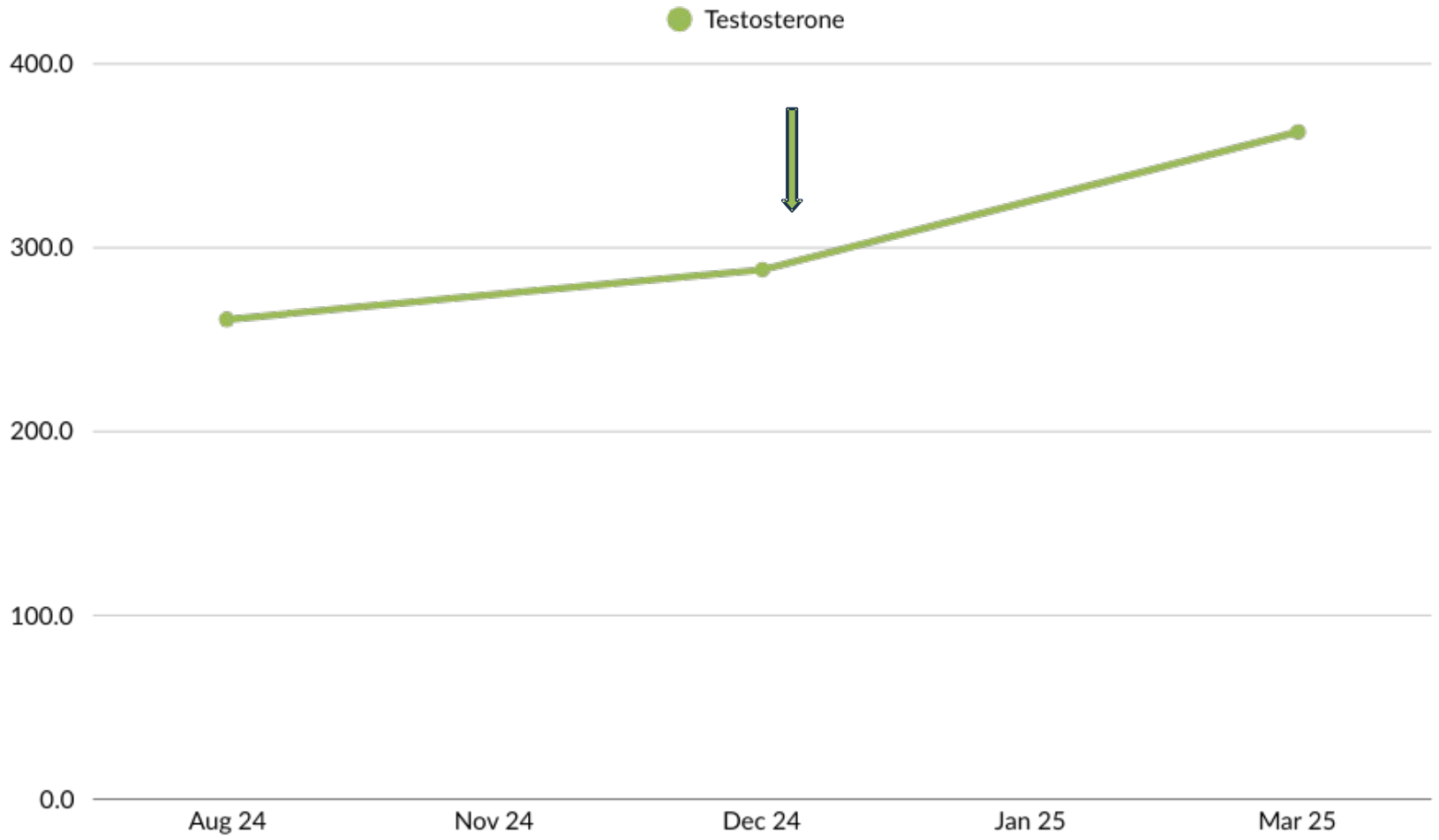
Magic Drug



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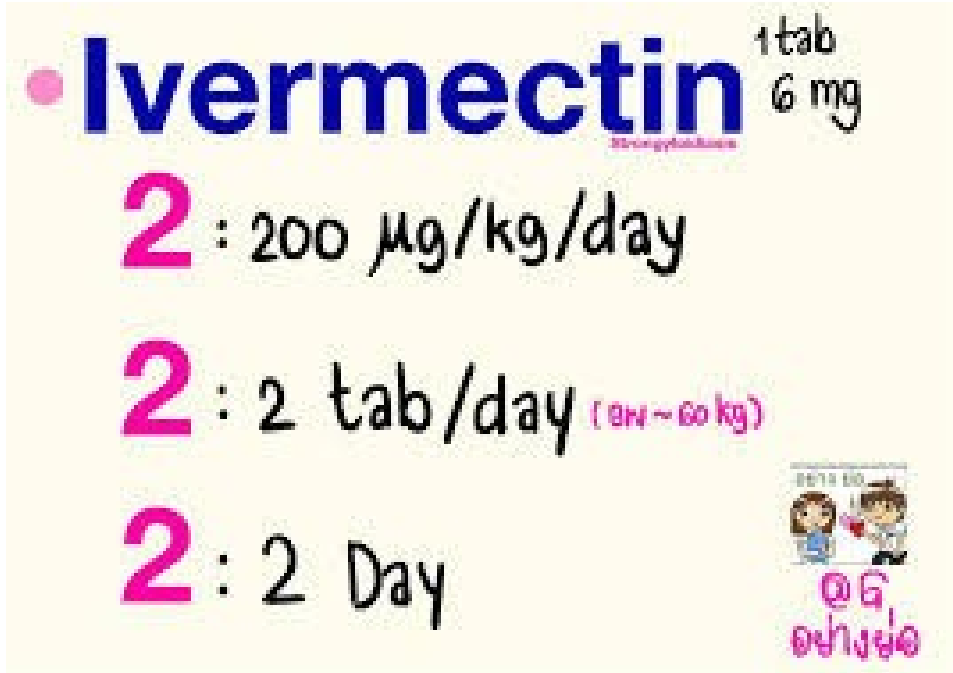

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