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The "Mad Protocol Syndrome." 7. A case of Cancer: The protocol to the end

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Jose Luis Turabian

Specialist in Family and Community Medicine.

Independent Researcher/Retired.

Formerly of the Health Center Santa Maria de Benquerencia. Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain.

***Corresponding author**: Jose Luis Turabian, Independent Researcher

Abstract

The "Mad Protocol Syndrome" is a condition in physicians who rigidly or normatively apply clinical guidelines or protocols. This syndrome, understudied but widespread, is seriously dangerous because it generates iatrogenic effects, promotes polypharmacy and drug interactions, is frequently based on controversial, unsound, and rapidly changing foundations due to the rapid emergence of new studies, fails to consider patient-centered care, is not developed collaboratively by medical specialties and patients, is often influenced by powerful interest groups (such as the relationship of almost all panelists on clinical guideline development committees with the pharmaceutical industry), always maintains an exclusively biomedical perspective ignoring broader biopsychosocial viewpoints, and because there are hundreds or thousands (or perhaps millions?) of clinical guidelines that contradict each other in their recommendations. The patient is a biographical, social, and spiritual reality, never an isolated analytical value. No laboratory target (HbA1c, LDL, or blood pressure) justifies destroying a human being's autonomy, lucidity, or daily well-being. "The Mad Protocol Syndrome" ultimately represents the dehumanization of medicine through bureaucracy. To break this absurd cycle of over-prescription and alienation, 21st-century medicine doesn't need to generate more guidelines from distant experts, but rather urgently reclaim the sovereignty of clinical judgment, safe deprescribing tools, and critical methodological approaches that return control to the primary care physician and dignity to the patient. Studying and reflecting on these concepts is the first step toward transforming clinical practice and rescuing the humane, critical, and sensitive medicine that patients so desperately need. Below is an example of clinical guidelines and protocols for A case of Cancer (Therapeutic obstinacy in advanced oncology; The protocol to the end).

Keywords: Guidelines; Methodology; Applicability, Evidence-based medicine; Patient-centered; Personalized medicine, General practice

Introduction

Clinical practice guidelines provide evidence-based recommendations to optimize patient care, while protocols dictate rigid, step-by-step procedures. In general medicine, these tools are designed to reduce practice variation and translate complex scientific research into actionable, patient-specific encounters (1, 2). However, clinical guidelines face significant systemic challenges. Key problems include a one-size-fits-all approach that fails to account for individual

variations, a lack of universal applicability, and potential conflicts of interest. Misuse of guidelines can sometimes lead to suboptimal care (3-5).

The concept we describe as the “Mad Protocol Syndrome” perfectly defines the phenomenon of the tyranny of clinical guidelines or normative biomedical reductionism.

This refers to the growing concern that modern medicine focuses too rigidly on treating isolated biological pathways and rigid, one-size-fits-all algorithms. This severely limits personalized care and ignores the complex, multifaceted realities of human illness (6).

In the scientific and critical medical literature, promoted by movements such as Choosing Wisely, evidence-based medicine without conflicts of interest, and quaternary prevention (7-10), there are blatant examples of guidelines that exhibit these characteristics: medicalization of risk factors, rigid objectives that induce massive polypharmacy in patients with multiple pathologies, a high rate of panelists with conflicts of interest with the pharmaceutical industry, and a complete disconnection from the biopsychosocial model. Here is an example of clinical guidelines and protocols for a case of Cancer (Therapeutic obstinacy in advanced oncology; The protocol to the end).

CLINICAL CASE: The "Mad Protocol Syndrome" Applied to Cancer (Therapeutic obstinacy in advanced oncology; The protocol to the end)

Andrew, 62 years old, with stage IV lung adenocarcinoma (metastatic to the liver and bones). He had progressed after three previous lines of chemotherapy and immunotherapy. He was very weak, spending 60% of the day in bed, with poorly controlled bone pain and severe anorexia (11).

The oncologist, observing on the CT scan that the tumors had grown by 20% (RECIST criteria) and seeing that Andrew could still walk to the clinic (ECOG 1-2), applied the scientific society's protocol: he initiated a fourth line of chemotherapy with a drug of high hematological toxicity. After the first cycle, Andrew suffered febrile neutropenia. He was admitted to the Intensive Care Unit, where he spent his last three weeks of life intubated, isolated from his family, and suffering the effects of multi-organ toxicity. He died under relentless medical intervention.

The "Mad Protocol" Approach:

Administering successive lines of chemotherapy, immunotherapy, or high-cost targeted therapies to patients with metastatic solid tumors in terminal stages, based solely on the patient meeting the criteria for "apparent good general condition" (ECOG score 0-1) and the RECIST criteria for tumor progression.

DISCUSSION

In Andrew's case, the doctor suffers from the "Mad Protocol Syndrome":

1) Iatrogenesis and polypharmacy: Forcing a fourth or fifth line of chemotherapy destroys the patient's last months of life due to hematological, renal, and digestive toxicity. A cascade of palliative drugs (antiemetics, corticosteroids, colony-stimulating factors, opioids) is added simply to control the side effects of the cancer treatment itself.

Forcing fourth or fifth lines of chemotherapy often leads to diminished returns and severe iatrogenic complications. In heavily pre-treated cancer patients, navigating polypharmacy and managing toxicities can significantly impair overall survival, physical function, and quality of life (12). The intersection of cancer treatment and polypharmacy presents

several documented clinical challenges (13) due to cumulative toxicity: Later-line chemotherapies typically offer lower response rates while introducing compounding, cumulative toxicities to bone, marrow, kidneys, and the liver (14); and due to drug-drug interactions (DDIs): Patients requiring four or five lines of chemotherapy are often on an extensive list of supportive medications. Polypharmacy (taking ≥ 5 medications) significantly increases the likelihood of hazardous DDIs. Research shows that polypharmacy is often independently associated with poorer survival and increased inpatient hospitalizations in patients undergoing systemic treatments (15).

2) Controversial and changing bases: Many new cancer drugs are approved by regulatory agencies through "accelerated pathways" based on surrogate endpoints (such as progression-free survival) that do not always translate into greater overall survival or a better quality of life for the patient. Research highlights several critical concerns regarding the use of surrogates such as Progression-Free Survival and Objective Response Rate (16-19).

3) Conflicts of interest: Oncology is one of the specialties under the greatest financial pressure globally. The authors of guidelines from major American (ASCO) and European (ESMO) societies have extensive connections with the biotechnology industry that funds clinical trials of these very expensive drugs. The intense financial strain on oncology, driven by skyrocketing drug costs and pharmaceutical-sponsored clinical trials, is heavily documented in the medical literature. Because guideline development involves experts who often have financial ties to the biotechnology industry, both the American Society of Clinical Oncology and the European Society for Medical Oncology actively maintain strict conflict of interest and disclosure frameworks to protect the integrity of their clinical recommendations (20).

4) Exclusive biomedical approach: Priority is given to chronic or "attacking" the tumor (millimeter reduction on CT scan), ignoring the biopsychosocial perspective: the patient's dignity, their desire to spend the end of their life at home without toxicity, and advance care planning for early palliative care (21).

What would a Patient-Centered Intervention Plan look like?

The doctor halts the active treatment algorithm. They sit down with Andrew and his family to develop an advance care plan. They honestly explain that more chemotherapy will not prolong his life, but it will destroy the quality of his remaining time. Active oncology is discontinued, and he is referred to early palliative care. The medical effort is focused entirely on pain management (adjusting opioids), emotional support, and ensuring Andrew' comfort at home. As a result, Andrew dies two months later in his bed, surrounded by his loved ones, without pain, maintaining his dignity, and having had the opportunity to say goodbye peacefully.

References

1. Panteli D, Legido-Quigley H, Reichebner C, et al. Clinical Practice Guidelines as a quality strategy. In: Busse R, Klazinga N, Panteli D, et al., editors. Improving healthcare quality in Europe: Characteristics, effectiveness and implementation of different strategies [Internet]. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2019. (Health Policy Series, No. 53.) 9. https://www.ncbi.nlm.nih.gov/books/NBK549283/
2. Conroy M, Shannon W. Clinical guidelines: their implementation in general practice. Br J Gen Pract. 1995;45(396):371-5. https://pubmed.ncbi.nlm.nih.gov/7612343/
3. Lau EW, Bonnemeier H, Baldauf B. Misuse of Guidelines Could Disadvantage and Harm Patients. J Evid Based Med. 2024;17(4):705-707. https://pmc.ncbi.nlm.nih.gov/articles/PMC11684497/
4. Dörenkamp S, Mesters I, Teijink J, de Bie R. Difficulties of using single-diseased guidelines to treat patients with multiple diseases. Front Public Health. 2015;3:67. https://pmc.ncbi.nlm.nih.gov/articles/PMC4413518/
5. Rapezzi C, Lorenzini M. How far should guidelines be followed? Eur Heart J Suppl. 2020;22(Suppl L):L121-L123. https://pmc.ncbi.nlm.nih.gov/articles/PMC7673602/
6. Cramer H. Whole Health Research Thought Further: How Can We Stay Whole in a Reductionist Paradigm? J Integr Complement Med. 2024;30(12):1123-1124. https://pmc.ncbi.nlm.nih.gov/articles/PMC11659440/
7. AbdulRaheem Y. Unveiling the Significance and Challenges of Integrating Prevention Levels in Healthcare Practice. J Prim Care Community Health. 2023;14:21501319231186500.https://pmc.ncbi.nlm.nih.gov/articles/PMC10350749/
8. Wagner H. Quaternary Prevention and the Challenges to Develop a Good Practice Comment on "Quaternary Prevention, an Answer of Family Doctors to Overmedicalization". Int J Health Policy Manag. 2015;4(8):557-8. https://pmc.ncbi.nlm.nih.gov/articles/PMC4529049/
9. Furlan L, Francesco PD, Costantino G, Montano N. Choosing Wisely in clinical practice: Embracing critical thinking, striving for safer care. J Intern Med. 2022;291(4):397-407. https://pmc.ncbi.nlm.nih.gov/articles/PMC9314697/
10. Martins C, Godycki-Cwirko M, Heleno B, Brodersen J. Quaternary prevention: reviewing the concept. Eur J Gen Pract. 2018;24(1):106-111. https://pmc.ncbi.nlm.nih.gov/articles/PMC5795741/
11. Gallegos K. [Clinical cases - medical oncology]. Slideshare. 2026. https://es.slideshare.net/slideshow/casos-clinicosoncologiamedica/247178063
12. Sharma M, Loh KP, Nightingale G, Mohile SG, Holmes HM. Polypharmacy and potentially inappropriate medication use in geriatric oncology. J Geriatr Oncol. 2016;7(5):346-53. https://pmc.ncbi.nlm.nih.gov/articles/PMC5037024/
13. Leporini C, De Sarro G, Russo E. Adherence to therapy and adverse drug reactions: is there a link? Expert Opinion on Drug Safety. 2014;13(sup1), 41–55. https://doi.org/10.1517/14740338.2014.947260
14. Baltussen JC, de Glas NA, van Holstein Y, et al. Chemotherapy-Related Toxic Effects and Quality of Life and Physical Functioning in Older Patients. JAMA Netw Open. 2023;6(10):e2339116. https://pmc.ncbi.nlm.nih.gov/articles/PMC10594146/
15. Hong S, Lee JH, Chun EK, et al. Polypharmacy, Inappropriate Medication Use, and Drug Interactions in Older Korean Patients with Cancer Receiving First-Line Palliative Chemotherapy. Oncologist. 2020;25(3):e502-e511. https://pmc.ncbi.nlm.nih.gov/articles/PMC7066695/
16. Pala L, Merlo F, Sala I, et al. Surrogate endpoints for overall survival in randomized clinical trials testing antibody-drug conjugates. J Natl Cancer Inst. 2025;117(8):1557-1564. https://pubmed.ncbi.nlm.nih.gov/40036179/

17. Gyawali B, Hey SP, Kesselheim AS. Evaluating the evidence behind the surrogate measures included in the FDA's table of surrogate endpoints as supporting approval of cancer drugs. EClinicalMedicine. 2020;21:100332. https://pubmed.ncbi.nlm.nih.gov/32382717/
18. Medical News. Study Highlights Inconsistencies in FDA Accelerated Approval Pathway for Cancer Drugs, MedPath. 2005; January 7. https://trial.medpath.com/news/study-points-to-weaknesses-in-fda-accelerated-approval-path
19. Shahnam A, Hitchen N, Nindra U, et al. Objective response rate and progression-free survival as surrogates for overall survival treatment effect: A meta-analysis across diverse tumour groups and contemporary therapies. Eur J Cancer. 2024;198:113503. https://www.sciencedirect.com/science/article/abs/pii/S0959804923008055
20. Mitchell AP, Dusetzina S, Basch EM. Financial ties to industry among national comprehensive cancer network guideline authors. J Clin Oncol. 2016; 34:6513-6513. https://ascopubs.org/doi/10.1200/JCO.2016.34.15_suppl.6513
21. Rodríguez U, Romar R. [Three patients and scientists star in an unprecedented event: "I decided that cancer couldn't stop my life"]. La Voz de la Salud. 2025; 25 feb. https://www.lavozdegalicia.es/noticia/lavozdelasalud/enfermedades/2024/11/06/decidi-cancer-parar-vida/00031730933620939237369.htm