Impact of Patient Personality on Adherence to Oral Anti-Cancer Medications: An Opportunity?

Mahtab Jafari, Alex Shahverdian, Gelareh Sadigh, Richard A. Van Etten

Submitted to: JMIR Cancer
on: February 16, 2024

Table of Contents

Impact of Patient Personality on Adherence to Oral Anti-Cancer Medications: An Opportunity?

Mahtab Jafari[1, 1] PharmD; Alex Shahverdian[1] PharmD; Gelareh Sadigh[2] MD; Richard A. Van Etten[3] MD, PhD

[1]Department of Pharmaceutical Scienes University of California, Irvine Irvine US
[2]Department of Radiological Sciences University of California, Irvine Orange US
[3]3 Chao Family Comprehensive Cancer Center University of California, Irvine Orange US

Corresponding Author:
Mahtab Jafari PharmD
Department of Pharmaceutical Scienes
University of California, Irvine
856 Health Sciences Quad 5400 Room 4020
Irvine
US

Abstract

Adherence to prescribed oral anticancer therapy is an important determinant of patient outcomes, including progression-free and overall survival. While many factors (e.g., medication side effects and out-of-pocket costs, problems with insurance authorization and timely medication refills) can affect adherence, one that is relatively unexplored is the impact of a patient's attitude and personality. Patient personality influences medication adherence and persistence in non-malignant chronic conditions such as cardiovascular disease and diabetes. In breast cancer and chronic myeloid leukemia, studies suggest that personality also affects adherence to oral chemotherapy which can be targeted to improve adherence. Here, we highlight the opportunity of incorporating patient personality as interventions to oral cancer therapy adherence, and discuss current barriers to implementation.

(JMIR Preprints 16/02/2024:57199)
DOI: https://doi.org/10.2196/preprints.57199

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Impact of Patient Personality on Adherence to Oral Anti-Cancer Medications: An Opportunity?

Mahtab Jafari[1], Alex Shahverdian[1], Gelareh Sadigh[2] ,and Richard A. Van Etten[3]

Affiliations
[1] Department of Pharmaceutical Sciences, University of California Irvine, Irvine, CA 92697, USA
[2] Department of Radiological Sciences, University of California Irvine, Orange, CA 92868, USA
[3] Chao Family Comprehensive Cancer Center, University of California Irvine, Orange, CA 92868, USA

Corresponding Author:
Mahtab Jafari, PharmD
Department of Pharmaceutical Sciences
3232 McGaugh Hall #3958
University of California, Irvine
Irvine, CA, 92697
Email: mjafari@hs.uci.edu

Abstract

Adherence to prescribed oral anticancer therapy is an important determinant of patient outcomes, including progression-free and overall survival. While many factors (e.g., medication side effects and out-of-pocket costs, problems with insurance authorization and timely medication refills) can affect adherence, one that is relatively unexplored is the impact of a patient's attitude and personality. Patient personality influences medication adherence and persistence in non-malignant chronic conditions such as cardiovascular disease and diabetes. In breast cancer and chronic myeloid leukemia, studies suggest that personality also affects adherence to oral chemotherapy which can be targeted to improve adherence. Here, we highlight the opportunity of incorporating patient personality as interventions to oral cancer therapy adherence, and discuss current barriers to implementation.

Keywords

cancer; medication adherence; medication persistence; personality, Five-Factor Model; Type D personality

Introduction

With acceleration in development of oral anti-cancer medications in recent years, a substantial number of patients with cancer are responsible for managing their medication. While oral anti-cancer medications have many advantages over parenteral chemotherapy including eliminating the need for venous access devices, many patients struggle with adhering to their prescribed regimens. Whereas medication adherence rates among patients with chronic diseases on oral treatment are estimated at approximately 50%, adherence rates for oral anti-cancer medications are substantially lower, with studies reporting adherence rates as low as 30% to 46% in patients with cancer [1-3]. Similarly, persistence to oral anti-cancer medications, defined as continuing treatment for the prescribed duration of therapy, is also suboptimal; for example, at 12 and 24 months, treatment persistence in patients with gastrointestinal stroma tumors and chronic myeloid leukemia

was reported to be 41% and 56%, respectively [4]. These are concerning statistics given that poor adherence to prescribed cancer therapy can lead to serious consequences such as disease progression, reduced treatment efficacy, increased symptom burden, an increased risk for recurrent cancer, and decreased overall survival [5-7].

Many patient-related factors can contribute to non-adherence and non-persistence to prescribed therapies, including health literacy [8], social determinants of health including food insecurity and housing instability [9], out-of-pocket medication costs [10,11], patient age [12,13], number of prescribed medications [14], and medication side effects [15-17]. However, the impact of patient personality has remained relatively underexplored [18-22]. In this viewpoint, we review literature on the impact of personality on medication adherence and argue that developing patient education that is tailored towards each individual patients' personality may improve anti-cancer medication.

Assessment of Personality types

The psychological literature frequently assesses personality using the Five Factor Model (FFM) [23]. Also known as the "universal" model, the FFM is one of the most empirically supported personality models to date and consists of five personality categories (**Table 1**): Openness, Conscientiousness, Extraversion, Agreeableness, and Neuroticism. An alternative model recognizes four personality types (ABCD) [24]. The original categories of Type A (competitive, ambitious) and Type B (patient, creative) were first defined and studied in patients with cardiovascular disease [25], and were subsequently expanded to include Types C (analytical, introverted) and D (anxious, negative). In particular, the Type D personality, a trait associated with negative emotions such as worry and lack of social interaction out of fear of disapproval (**Table 2**); [26-28]. The relationship between the FFM and ABCD personality models has not been fully defined, but Type D subjects display FFM traits ranging from neurotic introversion with relatively low conscientiousness to stable extroversion with relatively high consciousness [29]. The Eysenck personality theory recognizes personality traits across three dimensions: extraversion/introversion, neuroticism/stability, and psychoticism/superego [30], and is commonly assessed using the Eysenck Personality Questionnaire-Revised Short Scale (EPQ-RS) [31].

Impact of personality on medication adherence in cardiovascular disease and diabetes

Association between patient personality assessed by the Five Factor Model and medication adherence has been studied in patients with cardiovascular disease [32]. In a recent study, patient personality was measured using the Japanese Ten-Item Personality Inventory (TIPI-J) for evaluation of the "Big Five" personality traits. A twelve-item adherence scale measured medication compliance, health care provider collaboration, willingness to access medication information, and acceptance of needing to take medication. Having higher conscientiousness was significantly associated with greater medication compliance, patient-provider shared

decision-making, and willingness to access information about medications [32]. Conscientiousness has also been associated significantly with health-related quality of life, self-efficacy, and satisfaction with life in patients with cardiovascular disease [33]. The type D personality trait, a measure of low social interaction and negative affectivity, is frequently observed in patients with cardiovascular disease [34,35]. Type D individuals have significantly poorer medication adherence patterns in patients with myocardial infarction [36], heart failure [35,37], and acute coronary syndrome [38]. This is in addition to the type D personality being a significant predictor of mortality in patients suffering from coronary heart disease [34].

Another common disease where medication adherence and personality have been studied is diabetes. Low adherence is a known issue in diabetic patients, leading to increased adverse outcomes such as higher hemoglobin A1c (HbA1c) levels and peripheral neuropathy [39]. More recently, studies have investigated the role the Five Factor Personalities have in diabetes [40,41]. In one study, diabetics determined to possess the neuroticism trait based on the Eysenck Personality Questionnaire-Revised Short Scale (EPQ-RS) were significantly less likely to be adherent to medication in bivariate analyses. The authors hypothesized an indirect relationship between adherence and neuroticism mediated through neuroticism's association with a lack of social support and self-efficacy [40]. Another study also showed a significant negative relationship between neuroticism and adherence along with self-care behaviors [41], but found a significant positive relationship between agreeableness and adherence. Finally, conscientiousness has also been demonstrated to be significantly positively correlated to taking medications as prescribed in type 2 diabetics [42]. These trends are not exclusive to type 2 diabetes, as adolescents with type 1 diabetes who possessed the conscientiousness trait were significantly more adherent to insulin administration while those with the neuroticism trait showed a significantly negative correlation [43]. Like cardiovascular disease, type D personality has also been linked to poor medication adherence in type 2 diabetics [44,45] and to be associated with increased HbA1c [45].

Medication adherence and personality in patients with cancer

As in other chronic non-malignant diseases, non-adherence and non-persistence to oral anti-cancer medication can be associated with multiple patient-related factors, some of which may be specific to the type or stage of cancer diagnosis or the duration of the prescribed therapy. The behavioral impact that accompanies a diagnosis of cancer can also have significant effects on the personality of a patient [46-48]. Therefore, it is possible that some patients may adopt negative social and affective traits, such as those that define the type D personality. Relative to other chronic diseases like hypertension and diabetes, cancer therapy is unique in that patients are dealing with an imminent life-threatening condition with medications where the drug choices may be limited and the side effects are substantial. Indeed, many studies in cancer patients identify medication side effects to be a major factor contributing to poor adherence and persistence [3,49-51]. It follows that a patient's attitude and personality might have a major effect on coping with such symptoms. However, literature examining personality traits and adherence in patients with cancer is limited. A study that examined the link between the

Five Factor Model and adherence to outpatient cancer therapies suggested that the two personality types of Conscientiousness and Agreeableness correlated with increased adherence [52], but the specific types of cancer and treatments were not explored in detail. A review of psychosocial determinants of adherence to oral anticancer treatment also found high levels of distress (anxiety, depression) to be a major factor contributing to non-adherence [53].

Two cancer types where adherence has been studied in significant detail are early-stage breast cancer and chronic myeloid leukemia [7]. Patients with either of these vastly different malignancies share two characteristics: minimal symptoms arising from the cancer itself and the major impact of medication non-adherence on progression-free and overall survival. Patients with early-stage hormone-receptor positive breast cancer are frequently treated with oral medications targeting estrogen/progesterone signaling (adjuvant endocrine therapy; AET) following surgical management of the primary tumor. Non-adherence and non-persistence to prescribed AET have been shown in numerous studies to correlate with significantly reduced overall survival [54-56], particularly in black women [57]. Side effects of AET represent a major factor associated with non-adherence in this population [49,58,59]. Patient personality has not been studied explicitly as a factor in AET adherence, but other studies have identified anticipatory positive emotions [60] and lower depressive symptoms associated with greater social support [61] to be associated with increased adherence.

Therapy of chronic myeloid leukemia (CML) has been revolutionized by ABL1 tyrosine kinase inhibitors (TKIs) such as imatinib (Gleevec®). Most patients with CML achieve cytogenetic remission with TKI treatment [62,63] and enjoy age-adjusted normal life expectancy [64], but therapy must be lifelong for most patients [65]. Adherence and persistence to TKI therapy is of paramount importance to clinical outcomes of patients with CML, as missing just one dose a week is associated with suboptimal response [66] and treatment failure [67,68]. As a consequence, the factors associated with TKI adherence in CML have been studied extensively [69,70] and include out-of-pocket costs [71,72], long-term side effects [73,74], and dosing schedule [75]. In CML as in breast cancer, the impact of patient personality on medication adherence has been largely unexplored, but a recent study found that patients with either type A or type D (particularly negative affectivity) were more prone to TKI non-adherence [76].

Can patient personality be leveraged to improve medication adherence in patients with cancer?

Intuitively, many patient-related factors that influence medication adherence might be mitigated by patient education methods that are tailored to their personality or disposition. A patient's personality can inform differences in the way they think, behave and feel [77]. It can help predict their compliance with follow-up appointments, adherence to medications, and the tendency to accept and implement medical advice [78,79]. Moreover, the personality of a patient likely influences those patient-related factors in the first place, making

it an imperative area for providers to understand better. Patient education strategies that are tailored to include patient personality could play an important role by ensuring that the information received by the patient is conveyed in a way that is most effective. This may imply that adherence levels could be improved when provider interactions are tailored to meet the unique needs of each patient's personality and beliefs [7,19,53,80]. For example, patients who exhibit a 'neurotic' personality type could be more likely to experience negative emotions like irritability and anxiety following a cancer diagnosis, negatively impacting adherence [81]. A behavioral intervention strategy that acknowledges the patient's emotions and uses positive psychology techniques could prove helpful in this case [82]. For a patient who is extroverted or outgoing, allowing a safe and nonjudgmental space to share their opinions before educating them on their medication usage could ensure improved listening and adherence. Since extroverts thrive on being creative, they could also be empowered to take control of their own health and identify strategies that help them remember to take medications. It is important to note, however, that each of the five personality traits in the FFM represent a range between two extremes [23]. For instance, the extroversion trait represents a continuum between extreme extroversion and extreme introversion. In general, however, since most people lie at neither end of the spectrum but somewhere in between, multiple strategies for each patient's unique disposition would likely be more effective [23].

To this end, several recent studies in patients with breast cancer have utilized interventions focused on personal attitudes and values to increase adherence to AET [83,84]. Post-hoc analysis of a randomized controlled trial found relaxation training to be more effective than cognitive behavioral therapy in improving adherence to AET[85]. A remotely delivered intervention based on personal values demonstrated feasibility and acceptability and showed promise in improving AET adherence [86]. In CML, an education program tailored to individual patients based on interviews and a designed set of distinct adherence aids improved TKI adherence in a randomized trial [87]. However, most efforts to improve TKI adherence have relied on analysis of large data sets to identify interventions and lack patient-focused approaches [88]. To address this, we (the authors) have launched a clinical trial aimed at better understanding the correlation between patient personality (assessed via the FFM) and TKI adherence in patients with CML (ClinicalTrials.gov NCT06229860).

Before these strategies can be explored further in the real-world setting, existing FFM personality assessments currently used in cancer care or literature must be evaluated. Although assessments of patient personality often appear in medical records, they are usually one-sided remarks limited to terms such as "pleasant," "short-tempered," or "difficult" and portray a rather superficial and incomplete perspective, which can in turn lead to biased intuitions [89,90], suboptimal care, and poor adherence. Instead, a structured and validated approach should be adopted to provide a more reliable breakdown of personality. A recent study examined the utility of the 20-item Mini International Personality Item Pool (mini-IPIP) scale in adults with cancer and reported

potential validity of the tool in oncologic clinical settings [91]. Despite being a shorter version compared to other full versions of FFM personality measures, such as the NEO-Five Factor Inventory [92], the mini-IPIP has also been widely cited in studies including healthy adults and illustrated sufficient internal reliability across diverse population samples [93]. Since the mini-IPIP is a 20-item questionnaire with potential internal and external validity, the tool could be reasonably administered to cancer patients. To facilitate smooth patient-provider interactions, patients could be requested to complete these assessments during a patient intake process or prior to an appointment via patient portals to allow providers ample time to review their personality profiles and prepare as needed prior to an encounter.

Conclusion

Behavioral intervention studies that seek to address each personality type should be conducted to reinforce positive health behaviors and promote adherence. Instead of using a cookie-cutter approach to patient counseling, understanding each person's unique personality, and adopting communication strategies that encourage optimal adherence can improve oncologic patient care. However, further research is needed to evaluate the impact of personality-specific medication counseling on adherence to oral anti-cancer medications. This includes validation studies that confirm the reliability of personality assessments in cancer patients, as well as studies that explore the effectiveness of psychological behavioral techniques on adherence in different personalities. At the same time, there is enough data to encourage research in this direction. We strongly believe that incorporating personality into oncological care will redefine how we approach patient care as a whole, especially in this age where personalized care models like precision medicine are on the rise.

References

1. Greer JA, Amoyal N, Nisotel L, Fishbein JN, MacDonald J, Stagl J, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The oncologist 2016 Mar;21(3):354-376. PMID 26921292. doi: 10.1634/theoncologist.2015-0405
2. Burkhart PV, Sabaté E. Adherence to long-term therapies: evidence for action. J Nurs Scholarsh 2003;35(3):207. PMID 14667488. doi: 10.5144/0256-4947.2004.221
3. Salgado TM, Mackler E, Severson JA, Lindsay J, Batra P, Petersen L, et al. The relationship between patient activation, confidence to self-manage side effects, and adherence to oral oncolytics: a pilot study with Michigan oncology practices. Support Care Cancer 2017 Jun;25(6):1797-1807. PMID 28108821. doi: 10.1007/s00520-017-3584-0
4. Hohneker J, Shah-Mehta S, Brandt PS. Perspectives on adherence and persistence with oral medications for cancer treatment. J Oncol Pract 2011 Jan;7(1):65-67. PMID 21532814. doi: 10.1200/jop.2010.000076
5. Ganesan P, Sagar TG, Dubashi B, Rajendranath R, Kannan K, Cyriac S, et al. Nonadherence to imatinib adversely affects event free survival in chronic phase chronic myeloid leukemia. Am J Hematol 2011 Jun;86(6):471-474. PMID 21538468. doi: 10.1002/ajh.22019
6. Makubate B, Donnan PT, Dewar JA, Thompson AM, McCowan C. Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality. Br J Cancer 2013 Apr 16;108(7):1515-1524. PMID 23519057. doi: 10.1038/bjc.2013.116
7. McCue DA, Lohr LK, Pick AM. Improving adherence to oral cancer therapy in clinical practice. Pharmacotherapy 2014 May;34(5):481-494. PMID 24877187. doi: 10.1002/phar.1399
8. Schönfeld MS, Pfisterer-Heise S, Bergelt C. Self-reported health literacy and medication adherence in older adults: a systematic review. BMJ Open 2021 Dec 16;11(12):e056307. PMID 34916329. doi: 10.1136/bmjopen-2021-056307
9. Wilder ME, Kulie P, Jensen C, Levett P, Blanchard J, Dominguez LW, et al. The Impact of Social Determinants of Health on Medication Adherence: a Systematic Review and Meta-analysis. J Gen Intern Med 2021 May;36(5):1359-1370. PMID 33515188. doi: 10.1007/s11606-020-06447-0
10. Sadigh G, Switchenko J, Weaver KE, Elchoufi D, Meisel J, Bilen MA, et al. Correlates of financial toxicity in adult cancer patients and their informal caregivers. Support Care Cancer 2022 Jan;30(1):217-225. PMID 34255179. doi: 10.1007/s00520-021-06424-1
11. Dusetzina SB, Besaw RJ, Whitmore CC, Mattingly TJ, 2nd, Sinaiko AD, Keating NL, et al. Cost-Related Medication Nonadherence and Desire for Medication Cost Information Among Adults Aged 65 Years and Older in the US in 2022. JAMA Netw Open 2023 May 1;6(5):e2314211. PMID 37200029. doi: 10.1001/jamanetworkopen.2023.14211
12. Weingarten MA, Cannon BS. Age as a major factor affecting adherence to medication for hypertension in a general practice population. Fam Pract 1988 Dec;5(4):294-296. PMID 3068088. doi: 10.1093/fampra/5.4.294
13. Punnapurath S, Vijayakumar P, Platty PL, Krishna S, Thomas T. A study of medication compliance in geriatric patients with chronic illness. J Family Med Prim Care 2021 Apr;10(4):1644-1648. PMID 34123906. doi: 10.4103/jfmpc.jfmpc_1302_20
14. Kim SJ, Kwon OD, Han EB, Lee CM, Oh SW, Joh HK, et al. Impact of number of medications and age on adherence to antihypertensive medications: A nationwide population-based study. Medicine 2019 Dec;98(49):e17825. PMID 31804305. doi: 10.1097/md.0000000000017825
15. Leporini C, De Sarro G, Russo E. Adherence to therapy and adverse drug reactions: is there a link? Expert Opin Drug Saf 2014 Sep;13 Suppl 1:S41-55. PMID 25171158. doi: 10.1517/14740338.2014.947260

16. Tedla YG, Bautista LE. Drug Side Effect Symptoms and Adherence to Antihypertensive Medication. Am J Hypertens 2016 Jun;29(6):772-779. PMID 26643686. doi: 10.1093/ajh/hpv185

17. Peddie N, Agnew S, Crawford M, Dixon D, MacPherson I, Fleming L. The impact of medication side effects on adherence and persistence to hormone therapy in breast cancer survivors: A qualitative systematic review and thematic synthesis. Breast (Edinburgh, Scotland) 2021 Aug;58:147-159. PMID 34049260. doi: 10.1016/j.breast.2021.05.005

18. Zugelj U, Zupancic M, Komidar L, Kenda R, Varda NM, Gregoric A. Self-reported adherence behavior in adolescent hypertensive patients: the role of illness representations and personality. J Pediatr Psychol 2010 Oct;35(9):1049-1060. PMID 20430840. doi: 10.1093/jpepsy/jsq027

19. Theofilou P, Panagiotaki H. A literature review to investigate the link between psychosocial characteristics and treatment adherence in cancer patients. Oncol Rev 2012 Mar 5;6(1):e5. PMID 25992207. doi: 10.4081/oncol.2012.e5

20. Shahin W, Kennedy GA, Stupans I. The impact of personal and cultural beliefs on medication adherence of patients with chronic illnesses: a systematic review. Patient Prefer Adherence 2019;13:1019-1035. PMID 31303749. doi: 10.2147/ppa.S212046

21. Szabo G, Fornaro M, Dome P, Varbiro S, Gonda X. A bitter pill to swallow? Impact of affective temperaments on treatment adherence: a systematic review and meta-analysis. Transl Psychiatry 2022 Sep 2;12(1):360. PMID 36056016. doi: 10.1038/s41398-022-02129-z

22. Szabo G, Szigeti FJ, Sipos M, Varbiro S, Gonda X. Affective temperaments show stronger association with infertility treatment success compared to somatic factors, highlighting the role of personality focused interventions. Sci Rep 2023 Dec 11;13(1):21956. PMID 38081851. doi: 10.1038/s41598-023-47969-x

23. McCrae RR, John OP. An introduction to the five-factor model and its applications. J Pers 1992 Jun;60(2):175-215. PMID 1635039. doi: 10.1111/j.1467-6494.1992.tb00970.x

24. Kanten P, Gümüstekin G, Kanten S. Exploring the Role of A, B, C and D Personality Types on Individuals Work-Related Behaviors and Health Problems: A Theoretical Model. Int J Bus Manag Invent 2017;6(7):29-37. doi:

25. Friedman M, Rosenman RH. Association of specific overt behavior pattern with blood and cardiovascular findings; blood cholesterol level, blood clotting time, incidence of arcus senilis, and clinical coronary artery disease. J Am Med Assoc 1959 Mar 21;169(12):1286-1296. PMID 13630753. doi: 10.1001/jama.1959.03000290012005

26. Denollet J. Type D personality. A potential risk factor refined. J Psychosom Res 2000 Oct;49(4):255-266. 11119782. PMID 11119782. doi: 10.1016/s0022-3999(00)00177-x

27. Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med 2005 Jan-Feb;67(1):89-97. PMID 15673629. doi: 10.1097/01.psy.0000149256.81953.49

28. Mols F, Denollet J. Type D personality in the general population: a systematic review of health status, mechanisms of disease, and work-related problems. Health Qual Life Outcomes 2010 Jan 23;8:9. PMID 20096129. doi: 10.1186/1477-7525-8-9

29. De Fruyt F, Denollet J. Type D personality: A five-factor model perspective. Psych Health 2002;17(5):671-683. doi: 10.1080/08870440290025858

30. Matthews G, Gilliland K. The personality theories of H. J. Eysenck and J. A. Gray: A comparative review. Personality and Individual Differences 1999;26(4):583-626. doi: 10.1016/S0191-8869(98)00158-5

31. Eysenck SBG, Sybil BG, Eyesnk HJ, Barrett P. A revised version of the psychoticism scale. Personality and Individual Differences 1985;6(1):21-29. doi: 10.1016/0191-8869(85)90026-1

32. Adachi T, Tsunekawa Y, Tanimura D. Association between the Big Five personality traits and

medication adherence in patients with cardiovascular disease: A cross-sectional study. PloS one 2022;17(12):e0278534. PMID 36454925. doi: 10.1371/journal.pone.0278534

33. Tabernero C, Gutiérrez-Domingo T, Vecchione M, Cuadrado E, Castillo-Mayén R, Rubio S, et al. A longitudinal study on perceived health in cardiovascular patients: The role of conscientiousness, subjective wellbeing and cardiac self-efficacy. PloS one 2019;14(10):e0223862. PMID 31622377. doi: 10.1371/journal.pone.0223862
34. Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL. Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet (London, England) 1996 Feb 17;347(8999):417-421. PMID 8618481. doi: 10.1016/s0140-6736(96)90007-0
35. Wu JR, Song EK, Moser DK. Type D personality, self-efficacy, and medication adherence in patients with heart failure-A mediation analysis. Heart & lung : the journal of critical care 2015 Jul-Aug;44(4):276-281. PMID 25979573. doi: 10.1016/j.hrtlng.2015.03.006
36. Williams L, O'Connor RC, Grubb N, O'Carroll R. Type D personality predicts poor medication adherence in myocardial infarction patients. Psychol Health 2011 Jun;26(6):703-712. 21391133. PMID 21391133. doi: 10.1080/08870446.2010.488265
37. Wu JR, Moser DK. Type D personality predicts poor medication adherence in patients with heart failure in the USA. Int J Behav Med 2014;21(5):833-842. PMID 24198039. doi: 10.1007/s12529-013-9366-2
38. Molloy GJ, Randall G, Wikman A, Perkins-Porras L, Messerli-Bürgy N, Steptoe A. Type D personality, self-efficacy, and medication adherence following an acute coronary syndrome. Psychosom Med 2012 Jan;74(1):100-106. 22155940. PMID 22155940. doi: 10.1097/PSY.0b013e31823a5b2f
39. Zhang ZP, Premikha M, Luo M, Venkataraman K. Diabetes distress and peripheral neuropathy are associated with medication non-adherence in individuals with type 2 diabetes in primary care. Acta Diabetol 2021 Mar;58(3):309-317. PMID 33211180. doi: 10.1007/s00592-020-01609-2
40. Huang J, Ding S, Xiong S, Liu Z. Medication Adherence and Associated Factors in Patients With Type 2 Diabetes: A Structural Equation Model. Front Public Health 2021;9:730845. PMID 34805063. doi: 10.3389/fpubh.2021.730845
41. Hazrati-Meimaneh Z, Amini-Tehrani M, Pourabbasi A, Gharlipour Z, Rahimi F, Ranjbar-Shams P, et al. The impact of personality traits on medication adherence and self-care in patients with type 2 diabetes mellitus: The moderating role of gender and age. J Psychosom Res 2020 Sep;136:110178. PMID 32623192. doi: 10.1016/j.jpsychores.2020.110178
42. Skinner TC, Bruce DG, Davis TM, Davis WA. Personality traits, self-care behaviours and glycaemic control in type 2 diabetes: the Fremantle diabetes study phase II. Diabet Med 2014 Apr;31(4):487-492. PMID 24147848. doi: 10.1111/dme.12339
43. Wheeler K, Wagaman A, McCord D. Personality traits as predictors of adherence in adolescents with type I diabetes. J Child Adolesc Psychiatr Nurs 2012 May;25(2):66-74. PMID 22512523. doi: 10.1111/j.1744-6171.2012.00329.x
44. Li X, Zhang S, Xu H, Tang X, Zhou H, Yuan J, et al. Type D Personality Predicts Poor Medication Adherence in Chinese Patients with Type 2 Diabetes Mellitus: A Six-Month Follow-Up Study. PloS one 2016;11(2):e0146892. PMID 26894925. doi: 10.1371/journal.pone.0146892
45. Li X, Gao M, Zhang S, Xu H, Zhou H, Wang X, et al. Medication Adherence Mediates the Association between Type D Personality and High HbA1c Level in Chinese Patients with Type 2 Diabetes Mellitus: A Six-Month Follow-Up Study. J Diabetes Res 2017;2017:7589184. PMID 28280745. doi: 10.1155/2017/7589184
46. Dahl AA. Link between personality and cancer. Future Oncol 2010 May;6(5):691-707. PMID 20465385. doi: 10.2217/fon.10.31
47. McFarland DC, Morita J, Alici Y. Personality Disorders in Patients with Cancer. Oncology (Williston Park, NY) 2019 Oct 28;33(10):686510. PMID 31661154.

48. Chow PI, Shaffer KM, Lohman MC, LeBaron VT, Fortuna KL, Ritterband LM. Examining the relationship between changes in personality and depression in older adult cancer survivors. Aging Ment Health 2020 Aug;24(8):1237-1245. PMID 30939904. doi: 10.1080/13607863.2019.1594158

49. Henry NL, Azzouz F, Desta Z, Li L, Nguyen AT, Lemler S, et al. Predictors of aromatase inhibitor discontinuation as a result of treatment-emergent symptoms in early-stage breast cancer. J Clin Oncol 2012 Mar 20;30(9):936-942. PMID 22331951. doi: 10.1200/jco.2011.38.0261

50. Krikorian S, Pories S, Tataronis G, Caughey T, Chervinsky K, Lotz M, et al. Adherence to oral chemotherapy: Challenges and opportunities. J Oncol Pharm Pract 2019 Oct;25(7):1590-1598. PMID 30253725. doi: 10.1177/1078155218800384

51. Verbrugghe M, Verhaeghe S, Lauwaert K, Beeckman D, Van Hecke A. Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: a systematic review. Cancer Treat Rev 2013 Oct;39(6):610-621. PMID 23428230. doi: 10.1016/j.ctrv.2012.12.014

52. Lima MP, Machado WL, Irigaray TQ. Predictive factors of treatment adherence in cancer outpatients. Psycho-oncology 2018 Dec;27(12):2823-2828. PMID 30239056. doi: 10.1002/pon.4897

53. Kaptein AA, Schoones JW, van der Meer PB, Matsuda A, Murray M, Heimans L, et al. Psychosocial determinants of adherence with oral anticancer treatment: 'we don't need no education'. Acta Oncol 2021 Jan;60(1):87-95. PMID 33151764. doi: 10.1080/0284186x.2020.1843190

54. McCowan C, Shearer J, Donnan PT, Dewar JA, Crilly M, Thompson AM, et al. Cohort study examining tamoxifen adherence and its relationship to mortality in women with breast cancer. Br J Cancer 2008 Dec 2;99(11):1763-1768. PMID 18985046. doi: 10.1038/sj.bjc.6604758

55. Hershman DL, Shao T, Kushi LH, Buono D, Tsai WY, Fehrenbacher L, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat 2011 Apr;126(2):529-537. PMID 20803066. doi: 10.1007/s10549-010-1132-4

56. Eliassen FM, Blåfjelldal V, Helland T, Hjorth CF, Hølland K, Lode L, et al. Importance of endocrine treatment adherence and persistence in breast cancer survivorship: a systematic review. BMC cancer 2023 Jul 4;23(1):625. PMID 37403065. doi: 10.1186/s12885-023-11122-8

57. Dang TH, Forkan ARM, Wickramasinghe N, Jayaraman PP, Alexander M, Burbury K, et al. Investigation of Intervention Solutions to Enhance Adherence to Oral Anticancer Medicines in Adults: Overview of Reviews. JMIR cancer 2022 Apr 27;8(2):e34833. PMID 35475978. doi: 10.2196/34833

58. Demissie S, Silliman RA, Lash TL. Adjuvant tamoxifen: predictors of use, side effects, and discontinuation in older women. J Clin Oncol 2001 Jan 15;19(2):322-328. PMID 11208822. doi: 10.1200/jco.2001.19.2.322

59. Fleming L, Agnew S, Peddie N, Crawford M, Dixon D, MacPherson I. The impact of medication side effects on adherence and persistence to hormone therapy in breast cancer survivors: A quantitative systematic review. Breast (Edinburgh, Scotland) 2022 Aug;64:63-84. PMID 35609380. doi: 10.1016/j.breast.2022.04.010

60. Hurtado-de-Mendoza A, Carrera P, Parrott WG, Gómez-Trillos S, Perera RA, Sheppard VB. Applying the theory of planned behavior to examine adjuvant endocrine therapy adherence intentions. Psycho-oncology 2019 Jan;28(1):187-194. PMID 30353610. doi: 10.1002/pon.4931

61. Bright EE, Stanton AL. Prospective investigation of social support, coping, and depressive symptoms: A model of adherence to endocrine therapy among women with breast cancer. J Consult Clin Psychol 2018 Mar;86(3):242-253. PMID 29265835. doi: 10.1037/ccp0000272

62. Hochhaus A, Larson RA, Guilhot F, Radich JP, Branford S, Hughes TP, et al. Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. The New England Journal of Medicine 2017 Mar 9;376(10):917-927. PMID 28273028. doi: 10.1056/NEJMoa1609324

63. Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2022 update on diagnosis, therapy, and

monitoring. Am J Hematol 2022 Sep;97(9):1236-1256. PMID 35751859. doi: 10.1002/ajh.26642

64. Gambacorti-Passerini C, Antolini L, Mahon FX, Guilhot F, Deininger M, Fava C, et al. Multicenter independent assessment of outcomes in chronic myeloid leukemia patients treated with imatinib. J Natl Cancer Inst 2011 Apr 6;103(7):553-561. PMID 21422402. doi: 10.1093/jnci/djr060

65. Atallah E, Schiffer CA. Discontinuation of tyrosine kinase inhibitors in chronic myeloid leukemia: when and for whom? Haematologica 2020 Dec 1;105(12):2738-2745. PMID 33054106. doi: 10.3324/haematol.2019.242891

66. Noens L, van Lierde MA, De Bock R, Verhoef G, Zachée P, Berneman Z, et al. Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: the ADAGIO study. Blood 2009 May 28;113(22):5401-5411. PMID 19349618. doi: 10.1182/blood-2008-12-196543

67. Marin D, Bazeos A, Mahon FX, Eliasson L, Milojkovic D, Bua M, et al. Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib. J Clin Oncol 2010 May 10;28(14):2381-2388. PMID 20385986. doi: 10.1200/JCO.2009.26.3087

68. Ibrahim AR, Eliasson L, Apperley JF, Milojkovic D, Bua M, Szydlo R, et al. Poor adherence is the main reason for loss of CCyR and imatinib failure for chronic myeloid leukemia patients on long-term therapy. Blood 2011 Apr 7;117(14):3733-3736. PMID 21346253. doi: 10.1182/blood-2010-10-309807

69. Jabbour E, Saglio G, Radich J, Kantarjian H. Adherence to BCR-ABL inhibitors: issues for CML therapy. Clin Lymphoma Myeloma Leuk 2012 Aug;12(4):223-229. PMID 22633166. doi: 10.1016/j.clml.2012.04.002

70. Geissler J, Sharf G, Bombaci F, Daban M, De Jong J, Gavin T, et al. Factors influencing adherence in CML and ways to improvement: Results of a patient-driven survey of 2546 patients in 63 countries. J Cancer Res Clin Oncol 2017 Jul;143(7):1167-1176. PMID 28289895. doi: 10.1007/s00432-017-2372-z

71. Dusetzina SB, Winn AN, Abel GA, Huskamp HA, Keating NL. Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia. J Clin Oncol 2014 Feb 1;32(4):306-311. PMID 24366936. doi: 10.1200/jco.2013.52.9123

72. Winn AN, Keating NL, Dusetzina SB. Factors Associated With Tyrosine Kinase Inhibitor Initiation and Adherence Among Medicare Beneficiaries With Chronic Myeloid Leukemia. J Clin Oncol 2016 Dec 20;34(36):4323-4328. PMID 27998234. doi: 10.1200/jco.2016.67.4184

73. Eliasson L, Clifford S, Barber N, Marin D. Exploring chronic myeloid leukemia patients' reasons for not adhering to the oral anticancer drug imatinib as prescribed. Leuk Res 2011 May;35(5):626-630. PMID 21095002. doi: 10.1016/j.leukres.2010.10.017

74. Unnikrishnan R, Veeraiah S, Mani S, Rajendranath R, Rajaraman S, Vidhubala Elangovan GS, et al. Comprehensive Evaluation of Adherence to Therapy, Its Associations, and Its Implications in Patients With Chronic Myeloid Leukemia Receiving Imatinib. Clin Lymphoma Myeloma Leuk 2016 Jun;16(6):366-371.e363. PMID 27052853. doi: 10.1016/j.clml.2016.02.040

75. Santoleri F, Ranucci E, La Barba G, Colasanto I, Scaldaferri M, Cattel F, et al. Adherence, persistence and efficacy of dasatinib and nilotinib in the treatment of patients resistant or intolerant to imatinib with chronic myeloid leukemia in chronic phase: an Italian multicenter study over two years in real life. Curr Med Res Opin 2021 Mar;37(3):477-481. PMID 33459083. doi: 10.1080/03007995.2021.1876006

76. Rychter A, Miniszewska J, Góra-Tybor J. Personality traits favourable for non-adherence to treatment in patients with chronic myeloid leukaemia: role of type A and D personality. Biopsychosoc Med 2023 Jan 19;17(1):1. PMID 36658586. doi: 10.1186/s13030-023-00261-w

77. American Psychological Association. Personality2022. Available from: https://aww.apa.org. https://www.apa.org/topics/personality.

78. Axelsson M, Brink E, Lundgren J, Lötvall J. The influence of personality traits on reported adherence to

medication in individuals with chronic disease: an epidemiological study in West Sweden. PloS one 2011 Mar 28;6(3):e18241. PMID 21464898. doi: 10.1371/journal.pone.0018241

79. Cheli S, Lam WWT, Estapé T, Winterling J, Bahcivan O, Andritsch E, et al. Risk perception, treatment adherence, and personality during COVID-19 pandemic: An international study on cancer patients. Psycho-oncology 2022 Jan;31(1):46-53. PMID 34314560. doi: 10.1002/pon.5775

80. Birand N, Boşnak AS, Diker Ö, Abdikarim A, Başgut B. The role of the pharmacist in improving medication beliefs and adherence in cancer patients. J Oncol Pharm Pract 2019 Dec;25(8):1916-1926. PMID 30786821. doi: 10.1177/1078155219831377

81. Cook SA, Salmon P, Hayes G, Byrne A, Fisher PL. Predictors of emotional distress a year or more after diagnosis of cancer: A systematic review of the literature. Psycho-oncology 2018 Mar;27(3):791-801. PMID 29318702. doi: 10.1002/pon.4601

82. Ng W. Neuroticism and well-being? Let's work on the positive rather than negative aspects. J Positive Psychol 2012;7(5):416-426. doi: 10.1080/17439760.2012.709270

83. Pezzolato M, Marzorati C, Lanzoni L, Monzani D, Masiero MA, Pietrobon R, et al. Interventions to increase adherence to oral therapies in breast cancer patients: A systematic review based on the behavior change technique taxonomy. Psycho-oncology 2023 Oct;32(10):1481-1502. PMID 37571974. doi: 10.1002/pon.6203

84. Bright EE, Finkelstein LB, Nealis MS, Genung SR, Wrigley J, Gu HCJ, et al. A Systematic Review and Meta-Analysis of Interventions to Promote Adjuvant Endocrine Therapy Adherence Among Breast Cancer Survivors. J Clin Oncol 2023 Oct 1;41(28):4548-4561. PMID 37531593. doi: 10.1200/jco.23.00697

85. Ream ME, Walsh EA, Jacobs JM, Taub C, Lippman M, Schaefer-Solle N, et al. Brief relaxation training is associated with long-term endocrine therapy adherence among women with breast cancer: post hoc analysis of a randomized controlled trial. Breast Cancer Res Treat 2021 Nov;190(1):79-88. PMC9245682. doi: 10.1007/s10549-021-06361-x

86. Arch JJ, Crespi CM, Levin ME, Genung SR, Nealis M, Mitchell JL, et al. Randomized Controlled Pilot Trial of a Low-Touch Remotely-Delivered Values Intervention to Promote Adherence to Adjuvant Endocrine Therapy Among Breast Cancer Survivors. Ann Behav Med 2022 Aug 2;56(8):856-871. PMID 34410568. doi: 10.1093/abm/kaab118

87. Kekäle M, Söderlund T, Koskenvesa P, Talvensaari K, Airaksinen M. Impact of tailored patient education on adherence of patients with chronic myeloid leukaemia to tyrosine kinase inhibitors: a randomized multicentre intervention study. J Adv Nurs 2016 Sep;72(9):2196-2206. PMID 27113362. doi: 10.1111/jan.12978

88. Heiney SP, Sorrell M, Sheng J, Adams SA, Nelson K, Nguyen LA, et al. Interventions to Improve Adherence to Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia: A Systematic Review. Am J Clin Oncol 2021 Jun 1;44(6):291-298. PMID 33867480. doi: 10.1097/coc.0000000000000818

89. Park J, Saha S, Chee B, Taylor J, Beach MC. Physician Use of Stigmatizing Language in Patient Medical Records. JAMA Netw Open 2021 Jul 1;4(7):e2117052. PMID 34259849. doi: 10.1001/jamanetworkopen.2021.17052

90. Himmelstein G, Bates D, Zhou L. Examination of Stigmatizing Language in the Electronic Health Record. JAMA Netw Open 2022 Jan 4;5(1):e2144967. PMID 35084481. doi: 10.1001/jamanetworkopen.2021.44967

91. Perry LM, Hoerger M, Molix LA, Duberstein PR. A Validation Study of the Mini-IPIP Five-Factor Personality Scale in Adults With Cancer. J Pers Assess 2020 Mar-Apr;102(2):153-163. PMID 31403328. doi: 10.1080/00223891.2019.1644341

92. McCrae RR, Costa PT. A contemplated revision of the NEO Five-Factor Inventory. Personality and Individual Differences 2004;36(3):587-596. doi: 10.1016/S0191-8869(03)00118-1

93. Donnellan MB, Oswald FL, Baird BM, Lucas RE. The mini-IPIP scales: tiny-yet-effective measures of the Big Five factors of personality. Psychol Assess 2006 Jun;18(2):192-203. PMID 16768595. doi: 10.1037/1040-3590.18.2.192

Acknowledgments

Supported in part by a gift from the Kay Family Foundation.

Table 1: The Five Factor Personalities & Associated Adjectives

Personality	Adjectives
Openness	Artistic, curious, imaginative, insightful, original, and wide interests
Conscientiousness	Efficient, organized, planful, reliable, responsible, and thorough
Extraversion	Active, assertive, energetic, enthusiastic, outgoing, and talkative
Agreeableness	Appreciative, forgiving, generous, kind, sympathetic, and trusting
Neuroticism	Anxious, self-pitying, tense, touchy, unstable, and worrying

Adapted from [23]

Table 2: Characteristics of Type D Personality

Type D Traits
1. Tendency to experience negative emotions
2. Propensity to suppress the expression of emotions and behaviors in social contacts
3. Feeling of unhappiness, worry, irritability, and low self-esteem
4. Distance in social relations, introversion

Adapted from [26]