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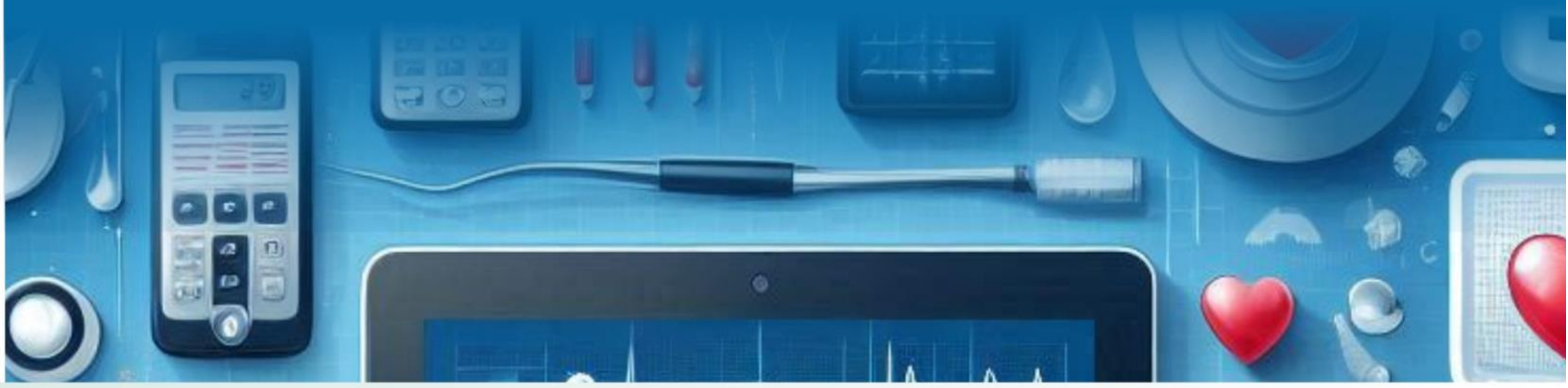

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Foreword

Prof. Nataliya Bhinder

Greetings to all readers of the Annals of Innovation in Medicine,

As we commence the first issue of the Annals for the year 2024, it is my privilege to introduce this latest compilation of groundbreaking research and transformative ideas in the field of medicine.

In a world where medical science is advancing at an unprecedented pace, the need for innovation in healthcare has never been more pressing. The Annals of Innovation in Medicine serves as a platform for disseminating cutting-edge discoveries, pioneering technologies, and visionary approaches that are shaping the future of healthcare delivery and patient outcomes.

Within these pages, you will find a diverse array of articles spanning a wide range of medical disciplines, each offering unique perspectives and insights into the challenges and opportunities facing modern medicine. From groundbreaking research studies to innovative clinical interventions, the articles in this volume represent the collective efforts of researchers, clinicians, and healthcare professionals dedicated to advancing the frontiers of medical knowledge and practice.

As editors, we extend our heartfelt appreciation to the authors for their invaluable contributions and to the reviewers for their diligent evaluation, which have ensured the quality and relevance of the published work.

To our esteemed readers, we invite you to explore the pages of the Annals with curiosity and an open mind. May the discoveries and insights contained herein inspire new ideas, foster collaboration, and ultimately lead to improved patient care and outcomes.

With warm regards,

Nataliya Bhinder

Editor-in-Chief

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Research Article

Effect of Exposure to Air Freshener on Hepatic Enzymes and Haematological Parameters of Albino Rats

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Abstract:

Air fresheners, which are available as incense sticks, scented candles, aerosols, liquids, gels, and electric diffusers, are used to mask odors with refreshing scents. They are widely used in homes, cars, and offices, marketed to create a clean and pleasant indoor atmosphere. However, many air fresheners contain volatile organic compounds (VOCs), which might have harmful effects on human health. This study evaluated the effects of exposure to a gel air freshener on hepatic enzymes and hematological parameters in albino rats. Thirty (30) albino rats, weighing 200-260g, were divided into three groups of ten rats each, and acclimatized for two weeks under 12-hour light/dark cycles with free access to food and water. Group I (Control) was not exposed to the air freshener, Group II was exposed to the air freshener for 4 hours daily for 28 days, and Group III for 8 hours daily for 28 days. After the treatment, the rats fasted overnight, were anesthetized with chloroform, and blood samples were collected via cardiac puncture. AST and ALT were assayed using enzymatic methods, and hematological parameters were measured with the Sysmex XP-300 Automated Haematology Analyzer (5-part). Results showed a significant increase ($p<0.05$) in AST, ALT, hematocrit, hemoglobin, red blood cells, and platelet levels in Group III compared to Groups I and II. No significant difference was found between Groups I and II. This suggests that 8-hour daily exposure to air freshener for 28 days induces hepatocellular damage and alters hematological parameters in albino rats, with the extent of damage increasing with longer exposure. However, further studies on humans are recommended.

Keywords: Air fresheners, hepatic enzymes, haematological parameters, aspartate aminotransferase, alanine aminotransferase, volatile organic compounds, inhalation exposure, liver damage

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1. Introduction

The adage "cleanliness is next to godliness" highlights the importance of a clean and pleasantly scented home, which exudes warmth and welcome. However, daily activities like cooking and pet care can result in lingering unpleasant odors. Air fresheners are commonly used to mask these odors, promoting a pleasant environment (1); (2). These products are prevalent in various indoor spaces, including offices, schools, hospitals, homes, and transportation modes, enhancing hygiene and sensory appeal. Despite their popularity, research indicates that air fresheners contribute significantly to indoor air pollution, posing health risks (3).

Air fresheners, which come in forms like incense sticks, scented candles, aerosol sprays, and electric diffusers, eliminate odors through chemical reactions or masking scents (3). However, they increase the number of odorous compounds rather than reducing air pollutants, often releasing over a hundred different chemicals, including volatile organic compounds

(VOCs) such as terpenes, benzene (4), formaldehyde, and phthalates (5), toluene (6), linalool (7). Despite their claims of creating a clean and sweet-smelling environment, many air fresheners contain harmful ingredients (2). These fumes when inhaled may trigger an immune reaction that involves the activities of blood cells and the detoxification function of the liver (1); (8).

These products release compounds linked to cancer, neurotoxicity, and endocrine disruption, thus affecting indoor air quality and potentially leading to health issues like eye, nose, and throat irritation, headaches, and damage to the liver, kidneys, and central nervous system (9); (2). Even at levels below accepted safety standards, chemical exposures from air fresheners can increase the risk of respiratory problems, such as asthma in children, and cause symptoms like dizziness and irritated eyes (2).

Figure 1: Some Brands of Air Refreshers

The liver, which is essential for nutrient metabolism and waste excretion, detoxifies foreign molecules and substances to reduce their toxicity (10), promoting their excretion through the intestines or kidneys. The critical role of the liver is evident in its ability to cause death if its functions are lost (11).

There is a scarcity of data on the evaluation of hematological parameters and hepatic enzymes following air freshener exposure. The only comparable study, conducted by (12), reported significantly elevated hepatic indices in rats exposed to air fresheners compared to the control group. Thus, conducting this study is essential to gain a deeper understanding of the changes in these parameters resulting from air freshener exposure. This study was aimed at evaluating the effect of exposure to air freshener on some liver enzymes and haematological parameters in albino rats.

2. Materials and Method

2.1 Purchase of Air fresheners and Test Kits

A brand of gel air freshener, named Sunshine air freshener, was randomly selected and purchased from Mile 3 Market in Port Harcourt, Rivers State, Nigeria. The air freshener was coded and stored at room temperature. The name, active ingredients, and expiry dates were recorded from the packages. Rat-specific test kits for AST and ALT, produced by Bioassay Technology Laboratory in Shanghai, China, were obtained from a local sales representative in Nigeria.

2.2 Ethical Considerations

The internationally accepted National Institutes of Health (NIH) Guide for Care and Use of Laboratory Animals were observed.

2.3 Experimental Animals

A total of 30 albino rats (both male and female), weighing between 200-260 grams, were sourced from the animal house at the Faculty of Pharmacy, University of Port Harcourt, Rivers State, for this study. The rats were kept in well-ventilated cages, maintained at a temperature of 27-30°C, with a 12-hour light/dark cycle. They had free access to tap water and dry rat pellets (bought at Mile 3 Market, Port Harcourt). The rats were randomly assigned to three groups of 10 rats each, and were allowed to acclimate for 28 days before the experiment began. After the animals adjusted to their surroundings, the experiment began. The first group (the control group) was not exposed to the air freshener, while the second and third groups (the test groups) were. The second group was exposed to the air freshener for 4 hours a day, every day for 28 days, while the third group was exposed for 8 hours a day, also for 28 days

2.4 Blood Sample Collection

After the 28 days of exposure to the air fresheners, the albino rats were allowed to fast overnight, after which they were anaesthetized in a jar containing cotton wool soaked in chloroform to render them unconscious. In this unconscious state, they were quickly removed from the jar, and 7ml of whole blood specimen was collected (using a sterile syringe and needle) through cardiac puncture into sterile sample containers; 4 ml was dispensed into plain bottles, which was spun at 3500rpm for 5 minutes to obtain the plasma which was in turn, used to analyze for AST and ALT using the rat-specific test kits, while the remaining 3ml of the blood specimen was dispensed into EDTA-anticoagulated bottles and was used to analyze for haematological parameters.

2.5 Sample Analysis

Enzymatic methods were used to measure the serum levels of AST and ALT (13). Hematological parameters were analyzed using the Sysmex XP-300 Automated Hematology Analyzer (5-part).

2.6 Statistical Analysis

The data generated from the analysis were expressed as Mean ± Standard Deviation and analyzed using the Statistical Package for Social Sciences (SPSS) version 26. Comparisons of mean and standard deviation values for various parameters between the test and control groups were made using one-way ANOVA and Tukey tests. Results were considered statistically significant at a 95% confidence interval ($p<0.05$).

3. Results

3.1 Comparison of the Levels of AST and ALT of Group I (Control), Group II, and Group III

Details of the comparison of the mean AST and ALT levels of the control (group I) and test (group II and group III) are shown in Table 3.1. The mean AST levels of group I, group II, and group III are 72.22±2.89 U/L, 71.07±7.21 U/L, and 89.20±10.85 U/L respectively, with the mean AST level of group III being significantly higher ($p=0.00001$) when compared with the mean levels of group I and group II. Similarly, the mean ALT levels of group I,

group II, and group III are 79.56±2.22 U/L, 89.90±12.52 U/L, and 108.65±11.06 U/L respectively, with the mean ALT level of group III being significantly higher (p=0.00001) when compared with the mean levels of group I and group II.

Table 3.1: Mean Levels of AST and ALT for Group I, Group II, and Group III Compared

GROUPS	AST (U/L)	ALT (U/L)
Group I (Control)	72.22±2.89	79.56±2.22
Group II	71.07±7.21	89.90±12.52
Group III	89.20±10.85[ab]	108.65±11.06[ab]
F-value	17.361	22.968
P-value	0.00001	0.00001
Remark	SS	SS

Key: SS – statistically significant, AST -Aspartate transaminase, ALT - Alanine transaminase, [a] – significantly different from Group I, [b] – significantly different from Group II

3.2 Comparison of the Levels of Haematological Parameters of Group I (Control), Group II, and Group III

Table 3.2 compares the mean levels of hematological parameters among the control group (group I) and the test groups (group II and group III). The mean WBC levels were similar across all groups, with no significant difference (p=0.400). However, group III showed significantly higher mean levels for several parameters compared to groups I and II. HCT: Group III (51.60±3.50%) was significantly higher (p=0.00001) than group I (40±4.22%) and group II (40.20±3.23%). HB: Group III (16.99±1.17 g/L) was significantly higher (p=0.00001) than group I (13.05±1.49 g/L) and group II (13.19±1.19 g/L). RBC: Group III (6.19±0.36 x10^{12}/L) was significantly higher (p=0.00001) than group I (4.31±0.53 x10^{12}/L) and group II (4.61±0.77 x10^{12}/L). Platelets: Group III (194±10.34 x10^{3}/µl) was significantly higher (p=0.030) than group I (182.90±7.40 x10^{3}/µl) and group II (182.70±13.14 x10^{3}/µl).

Table 3.2: Mean Levels of Some Haematological Parameters for Group I, Group II, and Group III Compared

GROUPS	WBC (X 10^{3}/µl)	HCT (%)	HB (g/l)	RBC X 10^{12}/L	PLATELET (X 10^{3}/µl)
Group I (Control)	5.66±0.41	40±4.22	13.05±1.49	4.31±0.53	182.90±7.40
Group II	5.65±0.28	40.20±3.23	13.19±1.19	4.61±0.77	182.70±13.14
Group III	5.86±0.44	51.60±3.50[ab]	16.99±1.17[ab]	6.19±0.36[ab]	194±10.34[ab]
F-value	0.949	32.707	30.008	30.512	4.025
P-value	0.400	0.00001	0.00001	0.00001	0.030
Remark	NS	SS	SS	SS	SS

Key: SS – statistically significant, NS – Not significant, WBC -White blood cell, HCT - Haematocrit, HB – Haemoglobin, RBC – Red blood cell, a – significantly different from Group I, b – significantly different from Group II

3.3 Correlation between Duration of Exposure and Liver Enzymes

Table 3.3 shows the correlation between the duration of exposure and liver enzyme activity: AST: A significant positive correlation (correlation coefficient = 0.627, p = 0.0002). ALT: A significant positive correlation (correlation coefficient = 0.783, p = 0.0002).

Table 3.3: Correlation between Duration of Exposure and Liver Enzymes

	Duration of Exposure (Years) vs. AST	**Duration of Exposure (Years) vs. ALT**
Pearson r	0.627	0.783
P value	0.0002	0.0002
Remark	SS	SS

Key: SS – statistically significant, NS – Not significant, AST -Aspartate transaminase, ALT - Alanine transaminase.

3.4 Correlation between Duration of Exposure and Haematological Parameters

Table 3.4 presents the correlation between the duration of exposure and hematological parameters. The findings are as follows: WBC: A nonsignificant positive correlation (correlation coefficient = 0.216, p = 0.251). HCT: A significant positive correlation (correlation coefficient = 0.735, p = 0.000004). HB: A significant positive correlation (correlation coefficient = 0.732, p = 0.000004). RBC: A significant positive correlation (correlation coefficient = 0.775, p < 0.001). Platelets: A significant positive correlation (correlation coefficient = 0.411, p = 0.024).

Table 3.4: Correlation between Duration of Exposure and Haematological Parameters

	Duration (Years) vs. WBC	**Duration (Years) vs. HCT**	**Duration (Years) vs. HB**	**Duration (Years) vs. RBC**	**Duration (Years) vs. PLATELET**
Pearson r	0.216	0.735	0.732	0.775	0.411
P value	0.251	0.000004	0.000004	<0.001	0.024
Remark	NS	SS	SS	SS	SS

Key: SS – statistically significant, NS – Not significant, WBC -White blood cell, HCT - Haematocrit, HB – Haemoglobin, RBC – Red blood cell

4. Discussion

This study aimed to assess the effects of exposure to a gel air freshener on liver enzymes (AST and ALT activities) and haematological parameters (white blood cells, haematocrit, haemoglobin, red blood cells, platelets) in albino rats. A significant increase in AST and ALT levels was observed in the group exposed to air fresheners for 8 hours daily (group III) for 14 days compared to the group exposed for 4 hours daily (group II) and the control group (group I) not exposed to air fresheners. Since AST and ALT are markers of hepatocellular injury, the results suggest that prolonged exposure to this air freshener may induce liver damage in rats, which may be attributed to the volatile organic compounds (VOCs) they contain

(14). These findings align with those of (15) and (1), who also reported elevated AST and ALT levels in albino rats exposed to air fresheners.

There was no significant difference in total white blood cell (WBC) count between the groups exposed to air fresheners (groups II and III) and the control group (group I). Air fresheners are known to contain VOCs (16), which are inhaled by the rats. This result suggests that WBC levels were not affected by these VOCs, contradicting previous studies that reported elevated WBC levels due to VOC exposure (17). However, the findings of this study contrast with those of (18), who reported a significant decrease in WBC levels in rats exposed to air fresheners. This discrepancy could be due to the use of liquid air freshener in their study, whereas our study employed a gel air freshener.

The rats exposed to air fresheners for 8 hours daily (group III) also showed elevated levels of haematocrit, haemoglobin, and red blood cells compared to the other groups. This increase might be due to higher erythropoietin production in response to hypoxia (19), indicating that air fresheners can reduce oxygen delivery to tissues, triggering a response to increase red blood cell production to compensate for the oxygen deficit. Furthermore, the platelet count was higher in the group exposed to air fresheners for 8 hours daily (group III), suggesting that VOCs might induce inflammation or other conditions leading to increased thrombopoietin production (16). The findings of this study also contrast with those of (18), who reported a significant decrease in the levels of red blood cells, haematocrit, and haemoglobin in rats exposed to air fresheners. Again, this discrepancy could be due to the use of liquid air freshener and rabbits in their study, whereas our study employed a gel air freshener.

The study also found a significant positive correlation between the duration of exposure to air fresheners and hepatic enzyme levels (AST and ALT), indicating that longer exposure leads to greater liver damage. Conversely, there was a nonsignificant positive correlation between exposure duration and WBC count, implying no effect on WBC levels. However, there was a significant positive correlation between exposure duration and other haematological parameters (haemoglobin, haematocrit, red blood cells, and platelets), suggesting that longer exposure increases these parameters.

5. Conclusion

This study demonstrates that exposing albino rats to a gel air freshener for 8 hours daily over 28 days resulted in elevated levels of hepatic enzymes AST and ALT, suggesting hepatocellular necrosis. In contrast, a 4-hour daily exposure for the same period did not significantly affect these enzyme levels. Regarding haematological parameters, the exposure did not alter total white blood cell levels. However, hemoglobin, hematocrit, red blood cells, and platelets levels were elevated after 8 hours of daily exposure for 14 days. Conversely, a 4-hour daily exposure for 28 days did not induce changes in these parameters. The study also reveals that increased duration of exposure to the air freshener correlates with higher AST and ALT levels, indicating greater hepatocellular damage. Additionally, longer exposure durations led to increased levels of hemoglobin, hematocrit, red blood cells, and platelets, indicating alterations in these hematological parameters.

References

1. Airaodion AI, Ogbuagu EO, Atiba FA, Olawoyin DS, Alabi OJ. Frequent exposure to air-freshener reduces male fertility. *Asian Research Journal of Gynaecology and Obstetrics*. 2020a;3(3):19-31.
2. Wickramasinghe AP, Karunaratne DGGP, Sivakanesan R. PM10-bound polycyclic aromatic hydrocarbons: biological indicators, lung cancer risk of realistic receptors and 'source-exposure-effect relationship' under different source scenarios. *Chemosphere*. 2012;87(11):1381-1387.
3. Kim S, Hong SH, Bong CK, Cho MH. Characterization of air freshener emission: the potential health effects. *The Journal of Toxicological Sciences*. 2015;40(5):535-550.
4. Smith MT. Advances in understanding benzene health effects and susceptibility. *Annual Review of Public Health*. 2010;31:133-148.
5. Steinemann AC. Fragranced consumer products and undisclosed ingredients. *Environmental Impact Assessment Review*. 2009;29(1):32-38.
6. Ono A, Kawashima K, Sekita K, Hirose A, Ogawa Y, Saito M, et al. Toluene inhalation induced epididymal sperm dysfunction in rats. *Toxicology*. 1999;139(3):193-205.

7. Aprotosoaie AC, Hăncianu M, Costache II, Miron A. Linalool: a review on a key odorant molecule with valuable biological properties. *Flavour and Fragrance Journal*. 2014;29(4):193-219.
8. Nørgaard AW, Kudal JD, Kofoed-Sørensen V, Koponen IK, Wolkoff P. Ozone-initiated VOC and particle emissions from a cleaning agent and an air freshener: risk assessment of acute airway effects. *Environment International*. 2014;68:209-218.
9. Mohammed B, Yakasai UA. Subacute toxicity study of some brands of air fresheners sold in Kano on Swiss albino rats (Rattus norvegicus). *Intl J Adv Acad Res| Sci, Technol & Engineer*. 2017;3:19-32.
10. Ibama O, C. Amadi F. Assessment of Serum Levels of Some Heavy Metals in Carpenters Residing in Port-Harcourt in Relation to Their Lifestyle. *Asian Journal of Research in Medical and Pharmaceutical Sciences*. 2018;4(4):1-7.
11. Ozougwa J, Eyo JE. Hepatoprotective effects of Allium cepa (onion) extracts against paracetamol-induced liver damage in rats. *African Journal of Biotechnology*. 2014;13:2679-2688.
12. Airaodion AI, Olawoyin DS, Alabi OJ, Atiba FA, Ogbuagu EO. Air freshener induced oxidative stress and its adverse effects on immunity. *International Journal of Health, Safety and Environment*. 2020b;6(5):579-587.
13. Reitman S, Frankel S. A colorimetric method of determination of serum oxaloacetate and glutamate transaminase. *Journal of Clinical Pathology*. 1957;28:56-58.
14. Cheville NF. Introduction to Veterinary Pathology. 3rd ed. Iowa State University Press; 2006. pp. 6-42.
15. Yakasai AU, Mohammed B. Biochemical effects of gel and liquid air fresheners sold in Kano on Swiss albino rats (Rattus Norvegicus). *Bayero Journal of Pure and Applied Sciences*. 2022;13(1):554-559.
16. Kim S, Lee AY, Cho MH. Inhaled exposure to air fresheners aggravated liver injury in a murine model of nonalcoholic fatty acid liver disease. *Heliyon*. 2021;7(3):1-7.
17. Akpan KV, Sogbanmu TO, Otitoloju AA. Effects of volatile organic solvents' inhalation on haematological and histological indices of Mus Musculus. *Current Advances in Environmental Science*. 2014;2(2):46-51.
18. Zuhair YA1-S. Hematological and biochemical effects of an air freshener in rabbits. *Journal of American Science*. 2012;8(8):70-73.
19. Ashade OO, Igbokwe L. Haematological and biochemical assessment of composite wood extracts in albino rat (Male Wister Strain). *Journal of Natural Sciences Research*. 2014;4(18):2224-3186.

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Case Report

Ureteral duplicity in a female patient with renal calculus in left UVJ- a case report

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Abstract: The ureters are tubular, bilateral, unique structures for each kidney, responsible for draining the urine collected in the renal pelvis to the bladder, so that it can later be eliminated. Ureteral duplication can be described as an abnormal urologic entity, with a frequency reported in 0.3 to 3% of the population. This anomaly is caused by the formation of double ureteral buds, which, in turn, form into separate structures and develop and form their own individual pelvic systems. A duplicated ureter is a result of early division of the ureteral bud into two or more completely or incomplete forms. Its diagnosis, for the most part, occurs incidentally, usually through imaging tests or even during surgery.

The objective of this study is to report a case of incomplete ureteral duplication and to highlight the type of treatment performed in the face of obstruction due to lithiasis.

Keywords: Obstruction, lithiasis, ureteral duplication, anomaly and UVJ, renal calculus

1. Introduction

The ureters are tubular, bilateral, unique structures for each kidney, responsible for draining the urine collected in the renal pelvis to the bladder, so that it can later be eliminated. Because they have smooth muscles in their embryological formation, the conduction of urine occurs through peristaltic movements, which, when associated with gravity, propel the urinary fluid towards the detrusor muscle (1).

Duplication of the ureter can be described as an abnormal urological entity, the reported frequency of which is 0.3 to 3% of the population (2). This anomaly is caused by the formation of double ureteral shoots, which in turn form in separate structures and develop into their own individual pyelocalial systems (1 and 2). The anatomical variations of the ureter and its relationship with adjacent structures are, therefore, important from an academic and clinical perspective, because when diagnosed, they can help in the maintenance and preservation of renal functions (2).

A duplicated ureter is the result of the early division of the ureteral bud into two or more completely (two ureters that drain into the bladder) or incompletely (two ureters that come together, forming a single ureter that drains into the bladder), known as a bifid ureter. (1, 2 and 3). In the meantime, duplicity of the ureter can be found in patients asymptomatically. However, it can be the cause of recurrent urinary tract infections (UTIs), urinary incontinence, vesicoureteral reflux, megaureter formation, urolithiasis, and pyelonephritis (1, 2, and 3).

Its diagnosis, for the most part, occurs incidentally, usually through imaging tests or even during surgery, whether by video or conventional (2 and 3). In the case of conventional

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surgeries, its presence, when not diagnosed, can cause the occurrence of medical iatrogenesis during the surgical procedure, due to the lack of recognition/identification of the structure(3).

2. Materials and Methods

The database used for the description of this report will be: the analysis of the medical record, the evolution, the laboratory tests and imaging tests performed, which were applied to determine the respective diagnosis of the patient in question

For a better understanding of the subject, previous studies on ureteral dupicity were used as bibliographic reference, which were made available in the PubMed, Scielo database and Capes/UNITAU portal.

3. Case report

Patient N. O. C., female, 25 years old, student, was admitted to the emergency room of the Regional Hospital of Vale do Paraíba with pain in the left flank region starting in the early hours of 07/23/2023. Associated with pain, she presented nausea and vomiting, but denied fever. He denies habitual use medications and allergies.

Previous pathological history: right ureterorenolithotripsy.

Physical examination: Good general condition, flushed, hydrated, eupneic, anicteric, acyanotic, afebrile. Cardiac system: Regular rhythm in 2 beats, normal sounds, no audible murmurs. Respiratory system: breath sounds present, no adventitious sounds. Abdomen: bowel sounds present, flaccid abdomen and painless on palpation, absence of masses or visceromegaly with normotympanic percussion, negative abrupt decompression, and negative giordano. Extremity: Peripheral pulses present and symmetrical, without cyanosis or edema, with capillary refill time less than 3 seconds.

Imaging test: CT scan of the abdomen 08/23/2023: presence of ureterolithiasis in the left ureterovasic junction (UVJ) with upstream dilation, 0.6 MM, absence of densification of ureteral and renal fat. Presence of incomplete double ureter on the left. (Image 1)

Conduct: rigid ureterorenolithotripsy + left to left double J catheter passage

Evolution: Surgical findings: presence of ureterolithiasis in left UVJ, fragmentation being performed by means of laser fiber, and removal of the fragments with Basket extractor forceps. The patient opted for the passage of a double J catheter on the left with a wire for removal. Confirmation of the diagnosis of incomplete double ureter intraoperatively by means of ascending pyelography and direct visualization. (Image 2)

Hospital discharge: Patient receives after diuresis and ambulation.

Return: Patient returns without symptoms, only for removal of the Double J catheter.

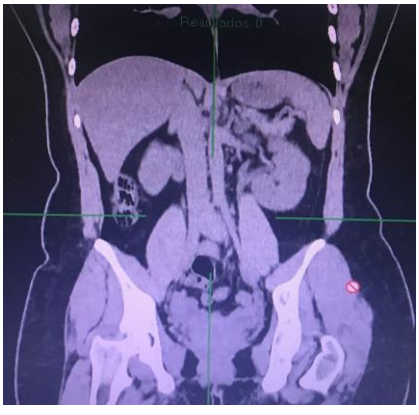

Image 1. CT scan: Presence of incomplete double ureter on the left.

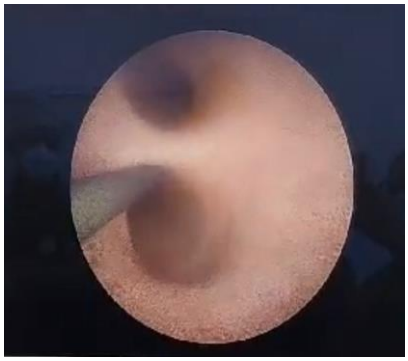

Image 2: ureteroscopy visualization intra-operatively.

4. Discussion

Ureteral duplication is a rare urological anatomical malformation, with a low incidence in the population, which may be associated with different types of pathologies.

There are two types of ureteral duplicity reported, complete and incomplete (bifid ureter) and are often accompanied by several complications. The latter is usually more associated with ureteroureteral reflux or obstruction of the ureteropelvic junction of the lower pole of the kidney, while the former has a higher incidence in females and is more frequently associated with vesicoureteral reflux, ectopic ureterocele, or ectopic ureteral insertion (1 and 5).

The diagnosis commonly occurs through an endourological procedure or imaging test performed to investigate the underlying cause of acute pain (3). The patient presented clinical symptoms of ureterolithiasis, which motivated her to seek specialized medical care. After being evaluated, a computed tomography scan was requested, confirming the diagnosis of ureterolithiasis in UVJ and also, incidentally, the presence of incomplete double ureter.

Imaging tests such as US and CT can be used to identify the presence of this type of anomaly, although they have low sensitivity and specificity (2 and 3). Radiological studies with the use of contrast, such as excretory urography and voiding cystourethrography, are the most indicated to promote a better understanding of preexisting anatomical structures (6). In addition, it is important to emphasize that minimally invasive ureteroscopy is also an effective option to treat ureteral and upper tract abnormalities (4), and is therefore the technique used to resolve the condition of the patient in this report and also to endoscopic confirmation of the diagnosis of ureteral duplicity.

5. Conclusions

Malformations of the urinary system should be kept in mind so that the correct and early diagnosis of this pathology can be made, since the lack of prior knowledge can lead to treatment complications.

In the reported case, the diagnosis was made previously, and the approach adopted brought excellent results with low morbidity.

References

1. Figueiredo, B. Q., et. Al. Bilateral complete ureteral duplication in a woman with recurrent urinary tract infection (UTI): case report. Research, Society and Development, v. 10, n. 12, e90101220174, 2021; (CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i12.20174
2. Balawender K, Pliszka A, Wysiadecki G, et al. Complete unilateral duplication of the right ureter with ectopic orifice to the prostatic urethra found by transrectal ultrasound. Pol Arch Med Intern 2022; 132: 16249. doi:10.20452/pamw.26249
3. Papageorgiou D., et al. Incomplete bilateral duplication of the ureters identified during cytoreductive surgery for ovarian cancer: A case report; International Journal of Surgery Case Reports 60; 2019; 213–215
4. Pedro, Renato N., et al. In Vitro Evaluation of Ureteral Perforation Forces. UROLOGY 70 (3), 2007
5. Hanson, G. R., Gatti, J. M., Gittes, G. K. & Murphy, J. P. (2007). Diagnosis of ectopic ureter as a cause of urinary incontinence. J Paediatr Urol., 3 (1): 53–57
6. Oge, O., Ozeren, B. & Sonmez, F. (2001). Nephron-sparing surgery in a duplex system associated with a vaginal ectopic ureter. Paediatr Nephrol.,16(3), 1135–1136.

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Case Report

Patient with cryptogenic cirrhosis

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Abstract: Cryptogenic cirrhosis is cirrhosis of uncertain etiology, with no definitive clinical and histological criteria for a specific disease. More than half of such patients are women, the average age is about 60, and patients generally have only mild liver enzyme abnormalities. Cryptogenic cirrhosis's pathophysiology is unknown; therefore, further research is required to elucidate the underlying etiology. The problem of liver cirrhosis is extremely important since this pathology occurs mainly in young and healthy people. In patients with cryptogenic cirrhosis, aminotransferase (AST and ALT) levels are usually only mildly elevated or normal. In our case report, a 41-year-old male patient was approved to the emergency department due to migraine pain. Liver enzymes were high in the blood analysis taken from the patient. As a result of the liver ultrasound carried out on the patient, it was reported to have decreased liver size and irregular boundaries and compatible with chronic liver disease. The patient used various analgesics due to migraine in his 20s. However, no cause could be identified for the patient's liver failure.

Keywords: Cryptogenic cirrhosis, NASH, ALT, AST, Liver failure

Introduction

Cryptogenic cirrhosis is cirrhosis of uncertain etiology, with no definitive clinical and histological criteria for a specific disease. Cryptogenic cirrhosis accounts for nearly 5% to 30% of cases of cirrhosis and nearly 10% of liver transplants. According to past studies, slightly more than half of such patients are women, the average age is about 60, and patients generally have only mild liver enzyme abnormalities. The pathophysiology of cryptogenic cirrhosis is unknown, and therefore, further research is required to elucidate the underlying etiology.

The problem of liver cirrhosis is extremely important since this pathology occurs mainly in young and healthy people. It also ranks among the top causes of death from digestive system diseases. Clinicopathological analysis of these patients indicates that leading causes include previously unrecognized nonalcoholic steatohepatitis, silent autoimmune hepatitis, viral hepatitis, and past occult ethanol exposure.

Nonalcoholic steatohepatitis (NASH) may account for many cases of cryptogenic cirrhosis. In patients with cryptogenic cirrhosis, aminotransferase (AST and ALT) levels are usually only mildly elevated or normal. This finding may be of particular relevance to cases resulting from NASH. The prevalence of NAFL/NASH parallels age, development of obesity, and type 2 diabetes.

Nonalcoholic fatty liver disease NAFLD refers to liver steatosis in patients with at least one metabolic risk factor (e.g., obesity, diabetes mellitus, dyslipidemia, hypertension). NAFLD may progress to cirrhosis and is likely an important cause of cryptogenic cirrhosis. The pathogenesis of NAFLD has not been fully established. The most widely supported theory suggests that insulin resistance is the key mechanism leading to liver steatosis and possibly steatohepatitis. Most patients with NAFLD are asymptomatic, although some patients may

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report fatigue, weakness, and discomfort in the right upper abdominal area. Asymptomatic patients are usually identified when laboratory testing shows elevated aminotransferases or when abdominal imaging shows liver steatosis as an incidental finding.

The complications of cryptogenic cirrhosis include the same complications that may be encountered with other causes of cirrhosis. These complications include hepatocellular carcinoma, hepatorenal syndrome, hepato-pulmonary syndrome, ascites, spontaneous bacterial peritonitis (SBP), and hepatic encephalopathy.

Case Report

A 41-year-old male patient applied for a control due to liver failure. The patient was approved to the emergency department due to migraine pain. Liver enzymes were high in the blood analysis taken from the patient. As a result of the liver ultrasound carried out on the patient, it was reported to have decreased liver size and irregular boundaries and compatible with chronic liver disease. He was referred to the hepatology polyclinic due to high liver enzyme values İn the blood analysis taken from the patient.

The patient used various analgesics due to migraine İn his 20s, had no alcohol use, and had no family history of liver disease. No viral hepatitis contamination was detected İn the blood tests.

HBSAG(MACRO) 0.45 Negative

ANTİ HIV(MACRO) 0.07 Negative

ANTİ HCV(MACRO) 0.08 Negative

ANTİ HBC TOTAL(MACRO) 0.1 Negative

Liver enzyme values are normal. In the abdominal ultrasound of the patient from a different hospital due to high ALP and GGT values, the liver parenchyma was clearly heterogeneous and coarsened, as well as its contours. It is lobulated (chronic liver disease?).

ALP 220

GGT 547

To investigate the etiology of the patient's liver failure, autoimmune hepatitis parameters were requested from the patient. All values were normal. Wilson tests were requested, but the results were normal.

ANA Negative

ASMA Negative

LKM Negative

Ceruloplasmin negative

A liver biopsy was requested from the patient, and there were no pathological results. The patient's Tomography and MRI results did not have any pathological conclusions other than chronic liver disease. Fat liver has not been detected. A portal vein Doppler was taken, and no pathology results were obtained. The patient's ALP and GGT values continued to be high İn all checks.

Latest results of the patient

ALP 157

GGT 372

No reason was found for the patient's liver failure. The patient has no active complaints and is clinically in good condition. He continues his routine checks.

Discussion and Conclusion

Cryptogenic cirrhosis is a common cause of liver-related morbidity and mortality. Non-alcoholic fatty liver disease (NAFLD) is now recognized as the most common cause of cryptogenic cirrhosis. However, in patients with NAFLD, cirrhosis is diagnosed later than other chronic liver diseases and, therefore, has a higher mortality rate. Definitive diagnosis requires a liver biopsy. Our 41-year-old male patient was approved to the emergency department due to migraine pain. Liver enzymes were high in the blood analysis taken from the patient. As a result of the liver ultrasound carried out on the patient, it was reported to have decreased liver size and irregular boundaries and compatible with chronic liver disease. The patient used various analgesics due to migraine İn his 20s, had no alcohol use, and had no family history of liver disease. No viral hepatitis contamination was detected İn the blood tests. A liver biopsy was requested from the patient, and there were no pathological results. No reason was found for the patient's liver failure. It is thought that the excessive and various analgesics used by the patient in his younger years may cause liver failure.

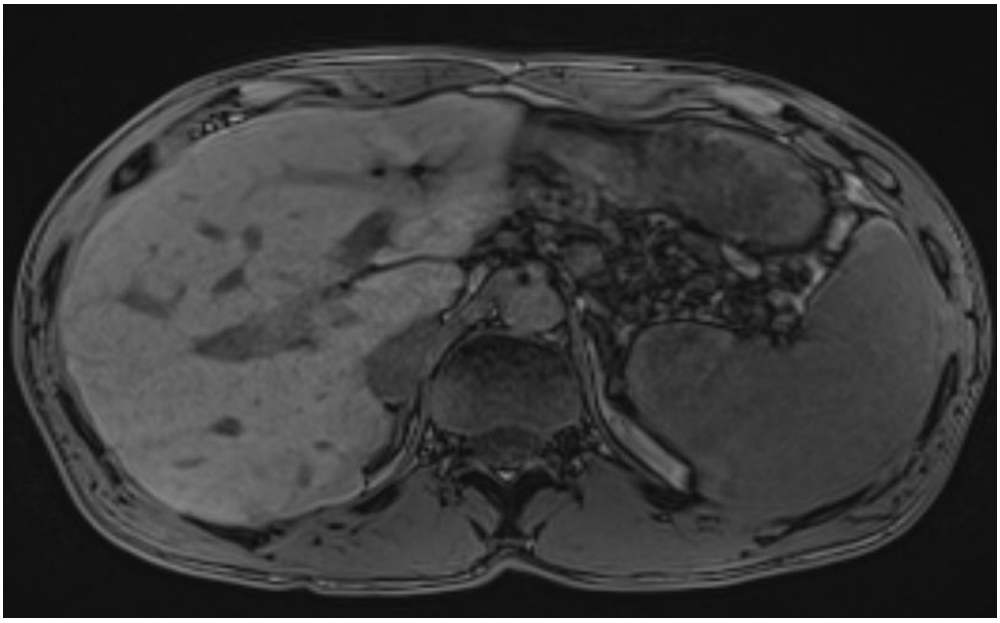

Figure 1: Decreased liver dimensions and irregular boundaries are observed on the patient's tomography.

References

1 Horlenko OM, Kossey GB, Pushkarenko OA, Prylypko LB. LIVER CIRRHOSIS WITH CRYPTOGENIC GENESES. CLINICAL CASE. Wiad Lek.
2 Yalamanchili K, Saadeh S, Klintmalm GB, Jennings LW, Davis GL. Nonalcoholic fatty liver disease after liver transplantation for cryptogenic cirrhosis or nonalcoholic fatty liver disease.
3 Caldwell S. Cryptogenic cirrhosis: what are we missing? Curr Gastroenterol Rep.
4 Xu X, Poulsen KL, Wu L, Liu S, Miyata T, Song Q, Wei Q, Zhao C, Lin C, Yang J. Targeted therapeutics and novel signaling pathways in non-alcohol-associated fatty liver/steatohepatitis (NAFL/NASH). Signal Transduct Target Ther.
5 Younossi ZM, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*
6 Arner P, et al. Adipose lipid turnover and long-term changes in body weight. *Nat.*
7 Patel N, Sharma B, Samant H. Cryptogenic Cirrhosis. 2023 Feb 12. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;
8 Clark JM, Diehl AM. Nonalcoholic fatty liver disease: an underrecognized cause of cryptogenic cirrhosis.

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Book Review

Book Review: The Comprehensive Cancer Centre: Development, Integration, and Implementation

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Keywords: Comprehensive cancer care, oncology infrastructure, cancer treatment, multidisciplinary approach, healthcare integration

Cancer has become one of most serious problems for public health, inducing a heavy economic burden on individual and national dimensions. An extensive scope of healthcare experts has unceasingly been making efforts to tackle this life-threatening illness. This edited volume, The Comprehensive Cancer Centre: Development, Integration, and Implementation, offers a platform to share the experiences and ideas from oncology studies across 18 chapters

with specialists from America, Asia, Europe, and the Middle East. Its objectives pertain to developing a comprehensive cancer care plan with guidance for hospitals and medical institutions and authorities, helping cancer centres upgrade their infrastructure, practice standards, policies and procedures aligning with the latest, highest international standards, especially for low- to middle-income countries, and exhibiting substantial measures for prevention, screening, diagnosis, treatment and rehabilitation in a sustainable and cost-effective manner.

Cancer care incurs voluminous direct and indirect costs; for instance, medical expenses and a loss of individual productivity, correspondingly. A mission-based comprehensive cancer care includes a variety of tangible and intangible arrangement, including physical settings, specialty roles, innovations and services, for which integrated delivery and novel therapies are necessary, with the aid of advanced support systems. High specialisation involves clinical care, multidisciplinary application, infrastructure, community outreach, education and training, and research. Such a care model also aims to diminish "financial toxicity" (p. 149), reduce healthcare inequality due to restricted resources, achieve better outcomes for cancer care and improved life quality for cancer patients, and increase survival rates. Eliminating disparities results in medical safety, welfare, social justice, and human rights.

A comprehensive cancer care centre offers inpatient and outpatient treatment and services. Inpatient ward settings and outpatient infusion centres need modern floor designs to ensure a clean and safe environment, in addition to paying attention to further staff training, facilities, and operational and financial management. Telecommunication technology sustains telepathology and telemedicine services, which promotes present trends in the contemporary healthcare field. Moreover, non-clinical care is also provided, such as palliative and hospice care (which encompasses physiological, social, psychological, emotional, mental and spiritual issues), and end-of-life counselling (which delivers adequate resources and guidance to patients who are suffering terminal illnesses or nearing death whether or not they are experiencing death anxiety).

Such a wide-ranging approach results in evidence-based, patient-centred care, with decreased readmissions to the hospital and enhanced patient satisfaction. It forms a complex of pathological services, intensive care, mental health and emotional disorders in order to look after the physical, psychological, and functional wellness of cancer patients. Therefore, extensive assistance is essential, regarding laboratories, blood banks, ancillary services for transplantation and transfusion, and biobanks to store biological samples for research, for which expertise, staff, placements, updated medical instruments, and a suitable health information technology system are heavily invested.

This complete spectrum of oncology care comprises survivorship care, including prevention, surveillance, intervention, and coordination. Community outreach becomes an integral part, providing cancer education and resources, scheduling appointments, arranging transportation, navigating treatments, giving support during appointments, and helping with financial guidance. However, certain obstacles hinder faster progress: fragmented care delays diagnosis and treatment, information technology systems often lack big data, education and training are immature, and international and local governmental support does not suffice.

Despite the holistic view of this patient-oriented cancer centre presentation, this compilation overlooks care for care-givers and patients' family members who need clinical support when they play a critical role in taking care of critically ill patients, especially for paediatric oncology and for the aged population. Similarly, compassion fatigue among medical frontliners is always given limited attention, because of which service quality is possibly to deteriorate. There has also been little detailed discussion on pain management; for example, bone metastases, for which complementary and alternative therapy is likely effective.

Here are some suggestions for ameliorating the readability of this book. First, promoting advanced medical directives is important for healthcare nowadays. This medical power of attorney allows patients to leave instructions on their healthcare preferences when they are still able to present their will and intended arrangements in order to ensure dignity and respect in death. Second, cultural and religious factors affect patients' values; hence, the outputs of this care model may vary among different groups. Although the authors do come from

various regions and countries, they could explore these factors more deeply. Third, even though outpatient cancer care during COVID-19 has been addressed in different chapters, there is a lack of in-depth examination; for example, on topics such as workplace safety, floor design and work flow, procurement, use of space in order to align with social and physical distancing, visits, and ward ventilation. Preparation for a peak in infectious diseases should be a popular topic for cancer patients. Last, this review proposes a protocol to develop this care approach from a global perspective. This will not only help translational research to incorporate studies into healthcare practices, but also low- and middle-income countries to cope with cancer.

This compilation confers multi-specialty care, using a diversified service team with multimodality expertise: specialised physicians, nurses, case managers, oncology-specific psychiatrists, psychotherapists, pharmacists, radiologists, physiotherapists, occupational therapists, speech therapists, dieticians, social workers, religious practitioners, and financial planners. Being aided by these human service professionals, precision medicine or personalised medicine maximises the utilisation of healthcare resources for patient care, and optimises sustainable, interdisciplinary and high-quality service, attaining smarter targeted therapies and securing quality management in the sense of structure, process and outcome. Furnishing the practitioner with an all-round view, the book is a worthy resource for clinical and healthcare professionals, scientists, researchers, administrators and policy makers, pharmacy and laboratory service providers, students, patients, and caregivers, who are willing to equip themselves with cutting edge concepts and to accomplish social equity in medical services.

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Research Article

The End of Alzheimer's Disease: Nudging Strategies to Encourage Mass Participation in Clinical Trials

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Abstract: Characterized by amyloid plaques, tau tangles, and neuronal loss, Alzheimer's disease (AD) presents a significant public health challenge, with ever-growing prevalence due to an aging global population. By the time cognitive impairment is detected, the disease's pathology is already extensive and difficult to halt. Despite advances in research and drug development, participation in AD drug trials remains crucial for discovering effective treatments and preventive measures. This article explores how behavioral economics can be employed to raise global awareness about Alzheimer's, motivate individuals to undergo testing, and encourage involvement in experimental drug trials. By integrating nudging strategies with creative educational approaches, this study aims to increase support for AD research.

Keywords: nudging; behavioral economics; Alzheimer's disease

1. Introduction

Every three seconds, someone in the world develops dementia. As of 2020, over 55 million people globally are living with this condition. This figure is expected to nearly double every two decades, projected to reach 78 million by 2030 and 139 million by 2050. A significant portion of this increase will occur in developing countries. Currently, 60% of individuals with progressive cognitive decline reside in low and middle-income nations, a percentage anticipated to rise to 71% by 2050. The most rapid growth in the elderly population is occurring in China, India, and their neighboring countries in South Asia and the Western Pacific (ADI, 2024). Characterized by memory loss and other cognitive impairments, Alzheimer's disease (AD) constitutes the most common cause of irreversible dementia, involving neurodegenerative processes marked by the formation of amyloid plaques and neurofibrillary tangles. Current treatments primarily address symptoms rather than altering disease progression, though research continues into potential disease-modifying therapies, including drugs targeting amyloid and tau proteins. Early diagnosis and intervention are therefore crucial, with ongoing trials focusing on pre-dementia stages like mild cognitive impairment (MCI) to identify effective treatments before significant brain damage occurs (Korolev, 2014). This paper combines nudging and other behavioral principles with relevant research and creative strategies in order to emphasize how they can all be applied to increase engagement in Alzheimer's disease research and prevention efforts.

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Unlike cancer, which can sometimes be treated or even miraculously cured, or HIV, which can be managed with proper medication, Alzheimer's disease remains a significant challenge for specialists, presenting difficulties from early symptom recognition to the troubling distinctions between early- and late-onset forms. Since there is still no effective treatment, the medical community continues to grapple with the complex and unforgiving nature of AD in all its manifestations. Nonetheless, this fatal illness, the fifth-leading cause of death among Americans age 65 and older, should not be considered an inevitable part of aging (AA, 2023). The saying *not all people age in the same way* can therefore be understood in this context as *not all older people get Alzheimer's*. While menopause and andropause represent normal aspects of aging, Alzheimer's does not, although a worryingly large number of elderly individuals believe they are already destined to develop this disease.

A key symptom of Alzheimer's is difficulty remembering recently learned information, as brain cells deteriorate due to the buildup of two problematic proteins: beta-amyloid, in the spaces between nerve cells, and tau, inside them. Other potential causes include head injuries, depression, and hypertension, according to scientists (NIA, 2024). Obtaining an accurate diagnosis at an early age thus proves challenging, as individuals may display different symptoms, depending on whether they are in the early, middle, or late stages of the disease. Comprehensive medical evaluations are therefore required to confirm Alzheimer's, since relying on one or two independent tests can lead to misdiagnosis, which can devastate someone's life.

Over the years, the diagnostic criteria for AD have significantly evolved to focus on presymptomatic and pre-dementia stages, bridging the gap between prevention and treatment trials. One review discusses how improved diagnostic reliability can enhance preventive strategies, the transition from observation to action, and ongoing intervention studies. The paper thus emphasizes the need to understand cognitive impairment and risk factors from a life-course perspective and highlights new approaches such as targeting genetic and beta-amyloid biomarkers, as well as multidomain interventions. International efforts like IDAD and EDPI are therefore key for advancing prevention methodologies and conducting large-scale trials to address AD and dementia globally (Solomon et al., 2014).

Early-onset Alzheimer's disease, also known as younger-onset Alzheimer's, affects individuals in their 30s, 40s, or 50s, adding to the complexity of an already bewildering condition, characterized by plaques and tangles that damage and eventually kill nerve cells. Like the later-onset form, the former has no cure and only offers limited prophylactic treatments, which may be linked to autoimmune diseases such as diabetes or fibromyalgia (Mendez, 2019). Thus, one thing is certain: no herb, drug, or regimen can currently cure this deadly disease, so research continues.

2. Behavioral Economics and Nudging

Behavioral economics (BE) explores how psychological factors influence economic decision-making, thereby revealing that individuals often deviate from rational choices due to biases and heuristics. This interdisciplinary field basically combines insights from psychology and economics to understand and predict human behavior more accurately (Raj, 2024).

Health problems are increasingly recognized as behavioral issues rather than purely medical ones, with unhealthy behaviors accounting for a significant portion of premature deaths and poor adherence to long-term therapies. For HIV patients, adherence to antiretroviral therapy (ART) remains suboptimal despite financial incentives, which often prove costly and have only short-term effects. Recent studies, like HPTN065, show limited success with large financial rewards, thus emphasizing the need for alternative approaches. Hence, behavioral economics offers promising insights for improving ART adherence. Instead of relying solely on large financial incentives, BE suggests using small, frequent rewards, non-monetary incentives such as social norms and personal commitments, and effective communication strategies (Linnemayr & Rice, 2016). By focusing on how incentives are framed and delivered, and integrating BE principles, researchers can ultimately design more effective and cost-efficient interventions to enhance health behaviors.

Similarly, David Asch (2016) posits that traditional health incentive programs in U.S. workplaces often fall short because they do not account for the complexities of human behavior. While many programs rely on rational models of education and financial incentives to improve health outcomes, these methods often overlook the irrational ways people make decisions. Asch, too, argues that behavioral economics offers better strategies by understanding psychological biases and creating interventions more aligned with human behavior. For example, framing incentives as losses rather than gains can lead to significantly better outcomes, such as increased physical activity. Asch further suggests that employers can improve health incentives by incorporating behavioral economics principles, which emphasize making changes to how incentives are designed and communicated. Rather than just offering financial rewards, leveraging social incentives and simplifying choices can be more effective. He also points out that health incentives should be tailored to address both general wellness and specific chronic conditions to have a meaningful impact. On the other hand, as seen with testing for HIV or hepatitis, or vaccination campaigns, public response to calls for action might be lukewarm, even with financial incentives. To address this, a combination of financial incentives (compensation or rewards) and recognition incentives (thanking or praising) should be employed to encourage participation, given that recognizing and appreciating individuals' contributions can help foster a positive behavior pattern in populations (Ritchie, 2024).

In the context of Alzheimer's disease, behavioral economics can be instrumental in designing strategies to increase awareness and participation in drug trials. By applying principles such as nudging, which subtly guides individuals toward more beneficial behaviors without restricting their freedom of choice, researchers and policymakers can effectively motivate people to engage in preventive measures, seek early testing, and contribute to experimental drug studies. This approach can thus leverage behavioral insights to address the complexities of decision-making in health contexts, ultimately improving outcomes in Alzheimer's research and treatment. In other words, by incorporating behavioral economics concepts into the planning and execution of the drug trials, organizers can better address public concerns, motivate participation, and ultimately advance the research efforts against Alzheimer's disease.

Thaler & Sunstein (2008) introduced the concept of nudging, which draws from social psychology, in order to challenge traditional economic theories that assume individuals always make rational choices to maximize their welfare. Instead, the scholars propose that people often exhibit bounded rationality, which leads to biased decisions that may not align with their best interests. Thaler and Sunstein thus advocate libertarian paternalism, where governments can subtly design choice environments – referred to as choice architecture – so as to guide individuals toward better decisions without removing their freedom of choice. As such, libertarian paternalism seeks to guide individual decision-making by using subtle interventions known as nudges in order to promote welfare-enhancing choices without significantly restricting freedom. Rooted in the law and economics movement, this approach aims to suggest preferable options rather than impose restrictions, thereby preserving personal choice while encouraging beneficial outcomes. Although libertarian paternalism may not serve as an all-encompassing ethical framework, it provides a useful addition to public health ethics by offering a method for gently steering individuals toward better decisions while maintaining their autonomy (Ménard, 2010). A nudge is basically defined as any modification in the choice architecture that alters behavior predictably while preserving all options and not significantly changing economic incentives. Nudges can include tactics like adjusting default options, altering how choices are presented, or creating small incentives. The appeal of nudging therefore lies in its simplicity and low cost compared to legislative approaches. For instance, nudging strategies might involve making healthier food options more prominent in canteens or changing the default setting for organ donation to an opt-out system. The approach contrasts with regulatory actions, which might impose stricter measures such as banning smoking in public places or increasing taxes on alcohol and cigarettes (Rainford & Tinkler, 2011). As such, the nudge approach presents several benefits for public sector problem-solving, particularly in times of limited resources. The main advantage ultimately lies in its ability to guide individuals toward better choices without imposing direct regulations or significant economic changes, which makes it appealing to governments seeking cost-effective solutions. By subtly influencing the decision-making environment, nudges can thus encourage people to make healthier or more beneficial choices, potentially addressing various public health and behavioral issues (Rainford & Tinkler, 2011).

However, the nudge approach also faces criticism for being patronizing and invasive, given that it involves altering people's decision-making environments without their explicit awareness. Critics specifically argue that such methods encroach upon personal autonomy and privacy, their users treating individuals as though they were incapable of making rational decisions on their own. Additionally, there are concerns that nudges might not lead to long-term behavioral changes and could be less effective compared to more direct regulatory measures. For instance, while nudging strategies may lead to modest improvements in salt consumption, they may not achieve the significant reduction seen with comprehensive legislation. The effectiveness of nudging might also be limited if it neglects broader systemic issues such as poverty and inequality, which also influence behavioral patterns (Keogh, 2017; Wachner et al., 2021). Despite these concerns, governments are increasingly adopting nudging techniques in policy-making, as evidenced by initiatives from national Behavioral Insights Teams, which apply behavioral insights to areas like health and consumer behavior (Murayama, 2023).

Since the global acknowledgment of libertarian paternalism, researchers have been exploring the effectiveness of nudge and think strategies in encouraging civic behavior and enhancing public service delivery. Their experiments have utilized randomized control trials to assess various interventions, such as feedback on recycling rates and public pledges for charitable donations. For instance, feedback cards improved participation in food waste schemes, and public recognition combined with pledges significantly increased book donations. These findings suggest that nudge strategies can effectively influence behavior through subtle adjustments in the decision-making environment. On the other hand, the think approach, which promotes collective deliberation on controversial issues, also showed promise yet with limitations. Experiments involving online discussions revealed modest shifts in policy preferences and suggested that while online deliberation can engage politically interested individuals, it may not broadly influence the general public. Additionally, mixed results were observed in experiments comparing information versus discussion on organ donation, which indicates that while nudges can prompt immediate actions, they might need to be complemented by broader engagement strategies to achieve sustained behavioral changes (John et al., 2011). Overall, while nudge interventions have demonstrated efficacy in small-scale settings, think approaches highlight the potential for deeper public engagement, although they require more innovative and systemic implementation to be fully effective.

Future research should therefore explore how social interactions and psychological insights can further enhance health outcomes, moving beyond the limitations of traditional economic models. Ultimately, nudging can guide people toward making decisions that align with their best interests, particularly in the context of preventing and curing AD.

3. Research Insights

3.1. High-profile announcements

In 2015, Charlie Sheen publicly revealed that he was HIV positive, a disclosure driven by his frustration with being blackmailed over the secret he had kept for years. So profound and unexpected was the impact of his announcement that it sparked a significant increase in the purchase of at-home HIV testing kits, demonstrating how his candidness had a tremendous effect on public behavior. As one article aptly put it, Sheen's honesty was equivalent to the impact of seven World AIDS Days combined (Migala, 2017).

The case of Charlie Sheen's disclosure of his HIV status demonstrates the power of celebrities' personal announcements in influencing public behavior. Similarly, prominent figures speaking about their experiences with AD or advocating research participation can have a significant impact on public attitudes and engagement.

3.2. FDA Approval Controversies

Several years ago, despite internal disagreement and insufficient evidence of benefit, the FDA approved Biogen's Alzheimer's drug, Aduhelm (aducanumab), under a controversial accelerated approval process. The decision faced significant criticism from experts and led to investigations into the approval process and pricing. A council of fifteen FDA officials had earlier determined that another clinical trial was necessary, warning that premature approval

could lead to widespread use without clear benefit or potential harm. Despite this, the FDA collaborated unusually closely with Biogen, which some argued compromised regulatory integrity, resulting in the approval of a drug that showed minimal efficacy in trials and was associated with risks like brain swelling and bleeding. The approval has sparked widespread backlash, with major medical centers opting not to offer Aduhelm and professional organizations like the American Neurological Association still opposing the approval. The FDA justified the decision by citing the accelerated approval program, which allows drugs targeting serious diseases with few treatment options to be approved based on biomarker effects that are "reasonably likely to predict clinical benefit." This rationale was controversial as many Alzheimer's experts believe there is insufficient evidence linking amyloid plaque reduction, Aduhelm's primary action, to cognitive benefits. The FDA's handling of the approval process, including its close ties with Biogen and deviations from typical procedures, has remained under intense scrutiny ever since (Belluk et al., 2021).

In 2024, Biogen has finally decided to abandon its ownership rights to Aduhelm, the controversial Alzheimer's drug, and discontinue the clinical trial that the FDA had mandated to confirm the drug's efficacy. As the initial approval of Aduhelm was met with fierce criticism due to the weak evidence supporting its benefits, this decision concludes a contentious period marked by outrage over the FDA's approval process, which involved irregularities and close collaboration with Biogen, and concerns about the drug's safety risks, such as brain swelling and bleeding. The financial and practical impacts of Aduhelm have been significant. Initially priced at $56,000 annually, it was expected to be widely used, potentially straining Medicare's budget and generating substantial revenue for Biogen. However, Aduhelm's market performance was dismal, bringing in only $7.8 million in its first year and a half. Medicare's decision to limit coverage to patients in clinical trials further hindered its adoption. Despite Biogen's statement that their withdrawal was not due to concerns over safety or effectiveness, the company's revenue from Aduhelm has been negligible. As Biogen exits from Aduhelm, the rights will revert to Neurimmune, the original licenser. Biogen will continue to supply Aduhelm until its license is withdrawn in November 2024. However, patients in the confirmatory clinical trial will only receive prescriptions for the drug until May. Meanwhile, the Alzheimer's treatment landscape has shifted, with new drugs like Leqembi from Biogen and Eisai, and donanemab from Eli Lilly, showing evidence of slowing cognitive decline, although their effects may not be significantly noticeable to patients (Robbins, 2024). This shift indicates a move toward more promising therapies in the battle against Alzheimer's disease.

The controversial approval of Biogen's Aduhelm highlights the complexities and challenges in drug approval processes, which can lead to a decline in trust in the regulatory process. By understanding these dynamics, nudging strategies can be designed to address concerns and build more trust in the research and approval processes. AD research has long acknowledged modifiable risk factors. *The Handbook of Prevention and Alzheimer's Disease* (2024) explores this field, known as the AD preventome, which now includes 12 risk factors potentially contributing to 40% of dementia cases globally. This new book educates on these factors and biomarkers, emphasizing their role in enhancing brain health and reducing AD risk while it also covers prevention domains like vascular health, social engagement, sleep, and spirituality (Raji et al., 2024). Alongside its companion volume on intervention, this recent study provides a comprehensive guide to strategies for preventing and addressing AD, useful for all professionals in the field.

Polygenic risk scores (PRS) are commonly used to predict disease risk by combining genetic markers, but they fail to capture the full heritability of complex diseases like late-onset Alzheimer's disease (LOAD) and lack generalizability across different populations. One significant study aims to improve LOAD risk prediction by developing a paragenic risk score that incorporates epistatic interaction features and machine learning methods. The new model enhances PRS by including interactions between SNP loci through an evolutionary algorithm and by using an ensemble of non-linear machine learning models to estimate risk. Compared to traditional PRS models, the paragenic model demonstrates significantly higher accuracy, achieving an AUC of 83% and matched sensitivity/specificity of 75% under 10-fold cross-validation, and maintains accuracy on independent datasets and within APOE genotype strata (Hermes et al., 2024). This approach shows promise for better predicting disease risk in complex heritable conditions like LOAD.

Unlike LOAD, early-onset Alzheimer's disease (EOAD) proves more heterogeneous, necessitating further exploration of its contributing proteins and pathways. Another very recent study used mass spectrometry to analyze cerebrospinal fluid (CSF) proteomics from a cohort of 139 samples – individuals with normal cognition, EOAD, and LOAD. Through correlation network analysis and machine learning, researchers identified differentially expressed proteins and associated pathways in EOAD, thus quantifying 2,168 CSF proteins and finding EOAD to exhibit more significant protein expression changes and synaptic dysfunction compared to LOAD. Three potential biomarkers for EOAD – SH3BGRL3, LRP8, and LY6H – were thus identified, with SH3BGRL3 accurately classifying EOAD in an additional Western cohort (Li et al., 2024). These findings offer a comprehensive CSF proteome profile for EOAD and highlight three promising biomarkers for early diagnosis.

3.3. Genetic Research Initiatives

Specialists remain perplexed by the causes of younger-onset Alzheimer's disease, especially what is now termed familial Alzheimer's disease, caused by rare deterministic genes inherited across multiple generations. This tragic reality affects many families in and around Medellín, the capital of Colombia's Antioquia province, although it also offers hope for a future cure. A particularly large family in Colombia, plagued by the rare genetic mutation E280A, has allowed researchers to study this mutation that predisposes them to Alzheimer's disease by age 45, ultimately leading to premature death. Owing to this research opportunity, Francisco Lopera, a clinical and behavioral neurologist at the University of Antioquia, and Kenneth S. Kosik, a neurologist and professor at the University of California, Santa Barbara, have developed an experimental drug, securing $15 million in grant funding from the National Institutes of Health (NIH) for a major trial. This antibody ultimately aims to clear beta-amyloid and prevent tau protein buildup, thereby preventing neuron death and the formation of deadly plaques and tangles. As a critical part of the project, 300 members of this extended family from Antioquia agreed to start testing the expensive medication several years ago (Hayes, 2017). They all carry the E280A mutation in the presenilin 1 gene, which makes them virtually certain to develop early-onset Alzheimer's disease. The participants are aged 30 to 60 and none have shown symptoms at the start of the trial.

The study, known as the Alzheimer's Prevention Initiative (API) Colombia Trial, proves one of the most ambitious and groundbreaking efforts to understand and potentially prevent AD. The drug under investigation is called crenezumab, developed by Genentech, a member of the Roche Group. Crenezumab is an antibody designed to bind to and clear amyloid-beta, a protein that accumulates in the brains of Alzheimer's patients. Participants are randomly assigned to receive either crenezumab or a placebo. The trial is double-blind, meaning neither the participants nor the researchers know who is receiving the actual drug versus the placebo. Participants receive injections every two weeks over a five-year period. The primary goal is to determine whether crenezumab can prevent or delay the onset of cognitive decline and dementia in people who are at genetic risk for Alzheimer's but are currently asymptomatic. Secondary measures include assessing changes in biomarkers related to Alzheimer's, such as amyloid plaques and tau tangles in the brain, through imaging studies and cerebrospinal fluid analyses. Besides NIH, the trial is funded by a combination of sources, including Banner Alzheimer's Institute, Genentech, and other organizations committed to Alzheimer's research (Reardon, 2018). The total funding for the project is therefore substantial, with significant contributions aimed at ensuring the trial's comprehensive nature and long duration.

However, the study faces several challenges, including ethical considerations of testing a drug on individuals who are not yet symptomatic but are certain to develop the disease. There is also the challenge of ensuring participant adherence to the trial protocol over the long term and managing the psychological impact of genetic knowledge on participants and their families. As of recent updates, the trial has been progressing, with researchers closely monitoring interim results (API, 2024). While complete results are not yet available, there is optimism in the scientific community about the potential findings, as the interim analyses are already helping determine the drug's safety and early efficacy signals. As a specific part of the project, the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease (API ADAD) Trial evaluated the efficacy of the anti-oligomeric amyloid beta antibody therapy crenezumab in cognitively unimpaired members of the Colombian presenilin 1 (PSEN1) E280A kindred.

The study outlines methods to ensure participant confidentiality and anonymity while making baseline data available to researchers. These methods included assessing potential risks, masking identifying variables, and implementing data management safeguards. Researchers can now request access to baseline demographic, genetic, imaging, clinical, and cognitive data, as baseline data are publicly accessible and future access to treatment data and biological samples will adhere to the original trial agreement and principles developed by the Collaboration for Alzheimer's Prevention. This data sharing aims to facilitate the exploration of crucial questions, such as the effects of starting investigational Alzheimer's prevention therapies before and after detectable amyloid plaque deposition (Reiman et al., 2023). This initiative is thus expected to advance Alzheimer's research significantly by making extensive trial data available to the scientific community.

Similarly, network hyperexcitability (NH) is emerging as a key pathophysiological process in early Alzheimer's disease (AD) and a potential treatment target. Functional connectivity (FC) measures have been proposed as biomarkers for NH, but their sensitivity in early-stage AD is unclear. An important study employs a whole brain computational model simulating progressive AD pathology to evaluate the performance of four FC measures: amplitude envelope correlation corrected (AECc), phase lag index (PLI), joint permutation entropy (JPE), and a novel phase lag time (PLT). The model replicates clinical spectral changes and NH progression. Results indicate that JPE and PLT are more sensitive than AECc and PLI in detecting early NH and AD-related abnormalities, suggesting that these novel FC measures could enhance early diagnosis and treatment targeting in AD (Stam & de Haan, 2024). Furthermore, recent developments suggest a realistic opportunity to develop, gain regulatory approval for, and implement effective preventive therapies in the near future. As such, intravenously administered anti-amyloid antibodies for secondary prevention may be available within three years, with subcutaneous self-administered therapies soon after, and subcutaneous antibody therapies for primary prevention potentially within five years (Reiman et al., 2024).

4. Testing and Drug Trials

The participation of people of different ages in testing crenezumab worldwide will significantly impact the medical field's efforts to stop and prevent Alzheimer's disease, so mass volunteering for drug injections proves crucial. Although such a revolutionary discovery might inspire people aged 30 to 65 to take action against Alzheimer's disease, this shift in consciousness cannot happen overnight or through individual efforts alone, especially when people are still healthy. Also, mass testing over many years will prove costly, necessitating close monitoring of participants globally and international collaboration, with periodic exchanges of results between researchers, along with constant feedback and brainstorming sessions. If future generations understand their pivotal role in combating and eventually eradicating Alzheimer's, the research process initiated with the Colombian family will continue seamlessly. By fostering global awareness and cooperation, the potential for significant advancements in preventing and treating AD will increase, which ensures that the groundbreaking efforts of the initial trial can be built upon and expanded worldwide.

As soon as all the side effects of the test drug have been addressed, the world will be provided with a safer and more effective antibody to prevent the formation of plaques and tangles in the brain, regardless of age. Therefore, the crucial behavioral shift needed is for adults to decide to participate in the mass testing of this experimental Alzheimer's medicine. Each country should establish testing centers in designated hospitals within cities where individuals can receive bi-weekly injections of the drug. These centers should be widely advertised through billboards, commercials, campaigns, and other forms of media, both inside and outside medical institutions, which can be facilitated by a responsible healthcare system working in conjunction with a proactive media industry. Additionally, organizing National Testing Days by Alzheimer's associations worldwide could help inform people about AD and the benefits of participating in drug trials.

In essence, global efforts will focus on raising awareness about the crucial role individuals in helping to cure Alzheimer's by participating in further testing of the experimental drug. However, encouraging people voluntarily to receive injections twice a month, especially when

they are asymptomatic, will be challenging. Overcoming fears of potential side effects and the discomfort of regular injections will require comprehensive education and reassurance about the drug's safety and the importance of mass contribution to medical research.

After mediatized communication of the research results from Colombia, this global initiative could be implemented across all countries simultaneously by using various methods of fostering collective participation in the AD drug testing: informing populations about Alzheimer's disease through leaflets, brochures, commercials, billboards, and similar channels; hosting workshops and seminars on AD and the benefits of drug trials; running constant campaigns against AD and promoting the benefits of drug trials; organizing National Testing Days, where people can meet others with the same disease or potential symptoms; conducting educational sessions in schools and workplaces, or even door-to-door initiatives; establishing support groups for participants in the drug testing to share their experiences; providing counseling and psychological support through NGOs to address issues and fears related to long-term testing; securing endorsements from officials or celebrities with influential authority; holding benefit concerts and other charity events to support testing centers; offering additional services through medical and governmental institutions (Parra et al., 2019; Sexton et al., 2021; Llibre-Guerra et al., 2023). These efforts aim to ensure widespread awareness and participation in the testing of the experimental Alzheimer's drug, emphasizing the importance of collective action in combating and potentially curing this disease.

A major challenge to this initiative is securing consistent grant funding for each participating country, given that sustaining the collective trial research project over many years requires substantial financial support, which no single health organization or National Institute of Health can provide indefinitely. Moreover, it is unrealistic and unethical to expect less developed countries to contribute financially on par with highly developed nations. To mitigate these challenges, several strategies could be implemented: developed countries and international organizations could pool resources to support less developed countries, thus ensuring equitable participation without financial strain and international disputes; engaging private sector stakeholders to contribute financially and logistically can also supplement public funding; international authorities can develop adaptable funding mechanisms that can be scaled up or down, based on the needs and capabilities of each country; clearly communicating the importance of the clinical trials and the potential long-term benefits can help garner public and governmental support; actively involving community leaders and influencers in promoting the initiative can enhance public trust and participation; rolling out the initiative in phases, starting with pilot programs in select regions worldwide, can help manage resources and demonstrate success before wider implementation (Cummings, 2019; ASPE, 2024).

In order to motivate individuals to participate in worldwide testing and experimental drug trials, the following personalized nudging strategies should also be considered: risk communication; simplified access; incentives and reminders. Thus, utilizing tailored communication strategies to convey the importance of early testing and trial participation and highlighting individual risk factors, such as genetic predispositions or lifestyle choices, can make the need for testing more relevant and urgent. Also, making the process of enrolling in trials as easy as possible can certainly remove barriers to participation. For example, streamlining registration procedures and offering trial information through easily accessible platforms can encourage more people to get involved. Additionally, providing small incentives, such as gift cards or public recognition, can motivate participation while using reminders and follow-ups can keep individuals engaged and informed about the trials.

Besides targeted nudging, organizers of large-scale drug trials should particularly consider several other concepts from behavioral economics and science to encourage effective participation and manage public perception:

Attribute Framing – Prospect Theory – Expected Utility (Rossiter, 2019)

The way drug trials are framed will significantly influence people's decisions. If the benefits and risks of participating are framed positively, emphasizing potential long-term gains and the proactive role in combating Alzheimer's, people may be more inclined to participate. Conversely, framing the trial in terms of risks or uncertainties might deter potential

participants. People's choices are often influenced by their anticipated utility values, which means that they weigh potential gains against potential losses.

Bounded Rationality vs. Rational Decision Making (Selten, 1990)

Acknowledging that individuals often operate under bounded rationality – limited cognitive resources and time – can help in designing the trials' communication strategies. While people may not always maximize their decision-making utility due to these limitations, they tend to use heuristics to make satisfactory decisions rather than optimal ones. Understanding this can help in crafting messages that simplify the decision-making process and make participation more appealing.

Loss Aversion – Risk Aversion – Status Quo (Kahneman et al., 1991)

People are generally more motivated by the fear of loss than by the potential for gain. They may therefore prefer to avoid the risk of participating in a drug trial due to fears of potential side effects, even if the trial offers a chance to prevent Alzheimer's disease. This aversion to risk and preference for maintaining the status quo can be addressed by clearly communicating the potential benefits and minimizing perceived risks. Emphasizing the safety measures and monitoring in place can also help alleviate fears.

Two Systems of Thinking (Kahneman, 2013)

Decision-making about participating in the drug trials will engage both System 1 (intuitive and emotional) and System 2 (deliberative and analytical) thinking. Initially, System 1 might lead to a quick, fearful response due to perceived risks. However, System 2 thinking, which involves more thoughtful consideration, might reveal the benefits and overall importance of the trials. Crafting messages that appeal to both systems can therefore help ensure that the decision to participate is well-informed and considered from both emotional and rational perspectives.

Information Avoidance – Inattention (Goldman, 2017)

People may choose to ignore information about Alzheimer's disease or the drug trials due to the belief that it does not concern them since they are currently healthy. To combat this, it is essential to create awareness campaigns that not only inform but also engage individuals on a personal level while indicating how participation could benefit them and others in the long run. Ensuring that information is accessible, relevant, and presented in a way that captures attention can thus overcome this avoidance.

Empathy Gap – Projection Bias – Social Conformity (HE, 2024)

Individuals often fail to appreciate future risks or benefits until they experience them directly. By highlighting personal stories and testimonials from those affected by AD, nudging can bridge this empathy gap, making the disease's impact more tangible. Also, people tend to underestimate their future risk of disease. Providing information about the growing prevalence of AD and the benefits of early participation in research can make anyone more aware of their potential future risks. As people are most often influenced by others' behavior, nudging can leverage social proof to encourage participation by showcasing high-profile endorsements or involving community leaders in promoting AD awareness.

Endowment and IKEA Effects (Norton et al., 2012)

Individuals value things more highly if they work with them and perceive them as their own. As such, by involving individuals in educational activities or trial-related events, such as community workshops or local fundraisers, authorities may help entire communities develop a stronger sense of ownership and commitment to AD research.

Thus, by addressing funding challenges and employing a multifaceted approach to incentivize participation, the global initiative could eventually achieve its goal of widespread involvement in Alzheimer's drug testing and research.

5. Increasing Awareness of Alzheimer's Disease

Owing to its potential to prevent, halt, and slow the progression of Alzheimer's disease, the drug crenezumab is currently being tested on perfectly healthy participants in Colombia. Of these, 200 carry the gene defect, while 100 do not. Furthermore, only 100 of the 200 are receiving the test drug every two weeks while the remaining 100 receive placebo injections. Researchers are hopeful that the drug will prevent the disease in those currently taking it, paving the way for further testing on individuals susceptible to Alzheimer's worldwide, both young and old. If completely successful, the drug could be taken preventively by everyone to ensure they never have to contend with this unforgiving disease (Hayes, 2017). However, this achievement will require many more years of trials, and larger sample sizes to expedite and improve the results.

While individuals already diagnosed with AD may not require additional motivation to participate in drug trials, healthy people, especially those in their 30s and 40s, will likely need more encouragement. Effective nudging, supported by concepts like the endowment effect (valuing what one already has) and the IKEA effect (placing higher value on things one helps create), can increase participation in drug testing. Family influence is also crucial, so authorities should consider creating a new animation franchise that educates and entertains people of all ages about AD. Cartoons have a broad appeal and can address serious issues in a relaxed and engaging manner, as seen with successful films like *Inside Out*, *The Incredibles*, *Zootopia*, and *Wall-E* (Bedekar & Prachi, 2020; Chakravorty & Tilak, 2021). Introducing a series like *The Alzhy Family Goes Nuts … or Not* could therefore be a novel approach. This fictional family, comprised of humorous guinea pigs, could represent the extended Colombian family initially involved in drug testing while honoring the animals used in research. Through relatable narratives, the storyline could explore various manifestations of early- and late-onset AD, educating, entertaining, and inspiring action all at once. It can thus provide information about Alzheimer's disease in a way that is accessible and engaging for all ages. Also, it can use humor and relatable characters to draw viewers in and make learning about AD enjoyable. Ultimately, it can motivate people to participate in drug trials by demonstrating the importance of the research and how it affects everyone.

All in all, introducing the name Alzhy /ˈæltsɪ/ in the context of a new animation series could foster a greater understanding of Alzheimer's disease while engaging a broad audience. Each episode could start with this explanation: *Alzhy is short for Alzheimer's disease, a name that honors all those who suffer from or are at risk of this condition*. This recurrent introduction would consequently help embed awareness of AD into viewers' minds at a subconscious level. The creative series, featuring *The Alzhy Family*, would air daily at child-friendly hours, providing a playful yet educational approach to understanding Alzheimer's. The guinea pig characters would navigate various scenarios illustrating AD-related challenges, including healthy living, brain health, symptoms of ad, medication and treatment. The Alzhies will eat healthily and do physical exercises to avoid obesity while undergoing brain tissue examinations and engaging in activities like reading, playing board games, solving puzzles, learning new skills. Some of the characters will still experience memory loss, difficulty walking or speaking, and other symptoms of early- or late-onset AD, and therefore they will take medication and participate in experimental drug trials.

Much like Tom and Jerry or Scrat in *Ice Age*, where characters face exaggerated mishaps in a humorous way, *The Alzhy Family Goes Nuts … or Not* would use humor to address the serious topic of AD. Given its emotional impact, this approach will render complex issues more accessible and engaging while episodes could integrate educational content about treatment and prevention strategies in a format both entertaining and instructive. Capitalizing on the success of the series, merchandise such as mugs, t-shirts, action figures, and shopping bags featuring The Alzhy Family could be developed, which will leverage the endowment and IKEA effects, making people more connected to the franchise through their physical possessions. To maximize the impact, some episodes could emphasize memorable and emotionally

powerful moments. This approach aligns with the peak-end rule, which suggests people can easily remember the most intense moments along with the end, which can influence their overall perception of an experience.

Thus, by integrating these elements into a comprehensive strategy, *The Alzhy Family Goes Nuts … or Not* could effectively use educational media and entertainment to increase awareness and participation in Alzheimer's disease research. The series would not only engage audiences but also foster a greater understanding of AD, motivating more people to contribute to research efforts and support drug trials.

6. School Experiments

For AD testing, schools in each country could use regular independent samples T-tests, which will compare the means for two classes of school children of different ages (data sets) of no more than 30 pupils or students each. The control group will be educated about AD in the classical way, through brochures, leaflets, workshops, seminars, for seven days in a row. The treatment group will watch each day, for a whole week, a different episode of the pilot series *The Alzhy Family Goes Nuts … or Not*. The goal of the study would be to determine if the observed results could be consistent across the entire population of a town or village, or merely random variations. The hypotheses for this comparison are as follows:

Null Hypothesis (H0): μwillingness to go drug testing 1 = μwillingness to go drug testing 2

Alternative Hypothesis (H1): μwillingness to go drug testing 1 ≠ μwillingness to go drug testing 2

To evaluate these hypotheses, school researchers could then calculate the T-score, which represents the ratio between the difference between the two groups and the variability within each group (Mishra, 2019). A large T-score indicates significant differences between the groups, while a small T-score suggests similarities. If the p-value is less than or equal to 0.05 (5%), the results will be considered statistically significant, meaning they are unlikely to occur by chance. Additionally, the standard deviation (SD) can be calculated to assess the dispersion of data around the mean (μ) and identify any outliers (Manikandan, 2011). This measure will help researchers understand the variability in participants' responses and make predictions about their behavior in real-world scenarios, such as their responsiveness to mass drug testing initiatives, particularly among young and healthy individuals.

Ultimately, the API ADAD trial in Colombia exemplifies how targeted research in genetically homogeneous populations can advance AD prevention efforts. By emphasizing the importance of participation in clinical studies, nudging can help drive engagement in similar trials globally, providing crucial insights into whether early intervention can alter the course of the disease, not just for those with the genetic mutation but also for the broader population at risk of late-onset Alzheimer's.

7. Conclusions

Alzheimer may be just an ordinary (and even beautiful) surname, but it carries an unfortunate association with a devastating medical condition, which arises from Alois Alzheimer's work in the early 20th century. Though the German psychiatrist and pathologist never intended to stigmatize others wearing it, his surname has become inextricably linked with a disease that claims millions of lives worldwide each year. Recognized as the most common and most feared type of dementia, Alzheimer's disease (AD) is directly linked to progressive cognitive decline and impairment, concentration difficulties, serious behavior problems, and memory loss – symptoms that develop gradually yet not slowly enough to be surpassed by the long-awaited lifesaving treatment. According to research, amyloid plaques, tau tangles, and neuronal loss are the most common causes of irreversible dementia, so early detection and participation in drug trials are critical for advancing research and finding effective treatments.

An extended family in Colombia presents a unique opportunity for researchers to explore the prevention of Alzheimer's disease, particularly due to their high prevalence of early-onset dementia linked to a rare genetic mutation, E280A, which guarantees Alzheimer's by age 45. This rare genetic defect led the affected Colombians to collaborate with local and international researchers, who secured substantial funding for a trial involving 300 family members. The study aims to test whether administering a drug to clear amyloid plaques before symptoms appear can prevent the onset of Alzheimer's. The trial's design aims to leverage the family's genetic homogeneity and their predictable disease onset, making it an ideal setting for testing preventive measures. Participants are split into groups receiving either the drug or a placebo, and will be monitored for many years to assess the drug's long-term effectiveness. The final results could transform Alzheimer's treatment by providing a method to halt or slow disease progression before symptoms develop, thus offering hope not only to those in the trial but also to later-onset Alzheimer's patients worldwide. If completely successful, the study could revolutionize the approach to preventing AD and shift current treatment paradigms.

However, motivating individuals, especially those without current symptoms, to participate in global trials can be challenging. This article discussed how key principles grounded in behavioral economics could effectively increase awareness, encourage testing, and drive participation in experimental drug trials. Thus, in addition to the various behavioral concepts and biases involved in encouraging mass participation in drug trials – such as attribute framing, loss aversion, empathy gap, and social conformity – employing nudging strategies will also increase participation in AD trials. In order to influence decision-making, nudging involves subtly guidance toward desired behavior by altering the environment in which choices are made yet without restricting individuals' freedom of choice.

The concept of nudging thus aims to steer people toward healthier choices without restricting their freedom, as it uses techniques such as changing the presentation of options or altering environments. While nudging is employed to improve public health outcomes – like promoting the reduction of unnecessary antibiotic use or implementing plain cigarette packaging – many debates center on the ethical implications of influencing choices without someone's awareness. Critics still argue that nudging can be controversial due to differing personal values and the complexity of health decisions, such as the trade-offs between medication benefits and side effects. To address these concerns, more transparent and explicit approaches, like shared decision-making and clear nudge strategies, are recommended. Individuals are therefore encouraged to question health recommendations and consider all options to ensure informed choices and balance the benefits and risks in light of personal values and preferences.

Nevertheless, behavioral nudges can offer a powerful toolkit for increasing awareness, encouraging testing, and driving participation in Alzheimer's disease research. For instance, introducing an animation series like *The Alzhy Family Goes Nuts … or Not* can combine education and entertainment, thereby creating engaging and informative media content that can effectively foster understanding of AD. Featuring a fictional family of guinea pigs navigating AD-related challenges, the series can educate viewers of all ages about brain health, symptoms of AD, and the importance of participating in drug trials. This approach leverages humor and relatability, making complex topics accessible and memorable. Moreover, by producing merchandise related to the animation series, such as t-shirts or mugs, viewers could feel a personal connection to the cause, which taps into the endowment and IKEA effects, as people are more likely to support causes in which they feel personally invested.

In the end, by integrating nudging principles with creative educational strategies, stakeholders could enhance public understanding of AD and foster greater involvement in experimental trials. As the prevalence of AD continues to rise, leveraging these behavioral insights can assist in advancing research and developing effective prevention and treatment strategies.

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References

ADI. (2024). Dementia statistics. Alzheimer's Disease International. https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/

Alzheimer's Association. (2023). 2023 Alzheimer's disease facts and figures. Alzheimer's Association Report, 14 March. https://alz-journals.onlinelibrary.wiley.com/doi/epdf/10.1002/alz.13016

API. (2024). The Alzheimer's Prevention Initiative (API) autosomal dominant Alzheimer's disease (ADAD) Colombia trial. Alzheimer's Prevention Initiative. https://alzheimerspreventioninitiative.com/api-studies/adad-colombia-trial/

Asch, D. (2016). Less logic, more health: How behavioral economics can improve incentives. Knowledge at Wharton. http://knowledge.wharton.upenn.edu/article/how-behavioral-economics-can-improve-health-incentives/

ASPE. (2024, April 22). National plan to address Alzheimer's disease: 2023 update. Office of the Assistant Secretary for Planning and Evaluation. https://aspe.hhs.gov/reports/national-plan-2023-update

Bedekar, M., & Joshi, P. (2020). Cartoon films and their impact on children's mentality. International Journal of Multidisciplinary, 5(6), 13-18. https://doi.org/10.31305/rrijm.2020.v05.i06.003

Belluck, P., Kaplan, S., & Robbins, R. (2021, July 19). How an unproven Alzheimer's drug got approved. The New York Times. https://www.nytimes.com/2021/07/19/health/alzheimers-drug-aduhelm-fda.html#:~:text=New%20Alzheimer's%20Disease%20Treatment%20Approved,that%20attacks%20the%20disease%20process

Chakravorty, D., & Tilak, G. (2021). Socio-cultural effects of visual representation through animated films with special reference to movies Inside Out & Zootopia. International Journal of Future Generation Communication and Networking, 14(1), 2636-2642.

Cummings, J. (2019). The role of biomarkers in Alzheimer's disease drug development. Advances in Experimental Medicine and Biology, 1118, 29-61. https://doi.org/10.1007/978-3-030-05542-4_2

Golman, R., Hagmann, D., & Loewenstein, G. (2017). Information avoidance. Journal of Economic Literature, 55(1), 96-135. https://doi.org/10.1257/jel.20151245

Hayes, K. (2017, July 14). Colombian family offers rare Alzheimer's research opportunity: Unique genetic mutation allows for preventive medicine trial. AARP. https://www.aarp.org/health/brain-health/info-2017/genetic-mutation-prevent-alzheimers-fd.html

HE. (2024). Heuristic Encyclopedia: Find everything you wanted to know about a heuristic. Newristics. https://newristics.com/heuristics-biases/empathy-gap

Hermes, S., Cady, J., Armentrout, S., O'Connor, J., Holdaway, S. C., Cruchaga, C., Wingo, T., & Greytak, E. M.; Alzheimer's Disease Neuroimaging Initiative. (2024). Epistatic features and machine learning improve Alzheimer's disease risk prediction over polygenic risk scores. Journal of Alzheimer's Disease, 99(4), 1425-1440. https://doi.org/10.3233/JAD-230236

John, P., Cotterill, S., Moseley, A., Richardson, L., Smith, G., Stoker, G., & Wales, C. (2011). Nudge, nudge, think, think: Using experiments to change civic behavior. Bloomsbury Academic. https://doi.org/10.5040/9781849662284

Kahneman, D., Knetsch, J. L., & Thaler, R. H. (1991). Anomalies: The endowment effect, loss aversion, and status quo bias. Journal of Economic Perspectives, 5(1), 193-206.

Kahneman, D. (2013). Thinking, fast and slow. Farrar, Straus and Giroux.

Keogh, B. (2017, October 11). Should you be 'nudged' into better health without you even knowing? The Conversation. https://theconversation.com/should-you-be-nudged-into-better-health-without-you-even-knowing-84601

Korolev, I. O. (2014). Alzheimer's disease: A clinical and basic science review. Medical Student Research Journal, 4, 24-33. http://msrj.chm.msu.edu/wp-content/uploads/2014/12/Fall-2014-Alzheimers-Disease.pdf

Li, D., Xie, Q., Xie, J., Ni, M., Wang, J., Gao, Y., Wang, Y., & Tang, Q. (2024). Cerebrospinal fluid proteomics identifies potential biomarkers for early-onset Alzheimer's disease. Journal of Alzheimer's Disease, 100(1), 261-277. https://doi.org/10.3233/JAD-240022

Linnemayr, S., & Rice, T. (2016). Insights from behavioral economics to design more effective incentives for improving chronic health behaviors, with an application to adherence to antiretrovirals. Journal of Acquired Immune Deficiency Syndromes, 72(2), e50-e52. https://doi.org/10.1097/QAI.0000000000000972

Llibre-Guerra, J. J., Heavener, A., Brucki, S. M. D., Marante, J. P. D., Pintado-Caipa, M., Chen, Y., Behrens, M. I., Hardi, A., Admirall-Sanchez, A., Akinyemi, R., Alladi, S., Dorsman, K. A., Rodriguez-Salgado, A. M., Solorzano, J., & Babulal, G. M.; Diversity and Disparity Professional Interest Area Increasing Sustained Diversity in Clinical Trials Working Group. (2023, July). A call for clinical trial globalization in Alzheimer's disease and related dementia. Alzheimer's & Dementia, 19(7), 3210-3221. https://doi.org/10.1002/alz.12995

Manikandan, S. (2011). Measures of dispersion. Journal of Pharmacology & Pharmacotherapeutics, 2(4), 315-316. https://doi.org/10.4103/0976-500X.85931

Ménard, J.-F. (2010). A 'nudge' for public health ethics: Libertarian paternalism as a framework for ethical analysis of public health interventions? Public Health Ethics, 3(3), 229-238. https://doi.org/10.1093/phe/phq024

Mendez, M. F. (2019). Early-onset Alzheimer's disease and its variants. Continuum (Minneap Minn), 25(1), 34-51. https://doi.org/10.1212/CON.0000000000000687

Migala, J. (2017, May 18). The Charlie Sheen effect on HIV testing was equivalent to 7 World AIDS Days. Vice. https://tonic.vice.com/en_us/article/wnwkab/the-charlie-sheen-effect-on-hiv-testing-was-equivalent-to-7-world-aids-days

Mishra, P., Singh, U., Pandey, C. M., Mishra, P., & Pandey, G. (2019). Application of student's t-test, analysis of variance, and covariance. Annals of Cardiac Anaesthesia, 22(4), 407-411. https://doi.org/10.4103/aca.ACA_94_19

Murayama, H., Takagi, Y., Tsuda, H., & Kato, Y. (2023). Applying nudge to public health policy: Practical examples and tips for designing nudge interventions. International Journal of Environmental Research and Public Health, 20(5), 3962. https://doi.org/10.3390/ijerph20053962

National Institute on Aging. (2024, January 19). What happens to the brain in Alzheimer's disease? National Institute on Aging. https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/what-happens-brain-alzheimers-disease

Norton, M. I., Mochon, D., & Ariely, D. (2012). The IKEA effect: When labor leads to love. Journal of Consumer Psychology, 22(3), 453-460.
Parra, M. A., Butler, S., McGeown, W. J., Brown Nicholls, L. A., & Robertson, D. J. (2019, December). Globalizing strategies to meet global challenges: The case of ageing and dementia. Journal of Global Health, 9(2), 020310. https://doi.org/10.7189/jogh.09.020310
Rainford, P., & Tinkler, J. (2011). Designing for nudge effects: How behavior management can ease public sector problems. The London School of Economics and Political Science. http://eprints.lse.ac.uk/37810/1/Designing_for_nudge_effects_%28lsero%29.pdf
Raj, N. (2024, April). Effects of behavioral economics on decision-making. In Transforming Business Practices in Changing Global Economy. Two-day International Conference organized by the School of Management and Commerce, ITM University Gwalior.
Raji, C. A., Leng, Y., Ashford, J. W., & Khalsa, D. S. (2024). Handbook of prevention and Alzheimer's disease. Advances in Alzheimer's Disease, 10. https://www.j-alz.com/
Reardon, S. (2018, March 27). Pioneering Alzheimer's study in Colombia zeroes in on enigmatic protein. Nature. https://www.nature.com/articles/d41586-018-03848-4
Ritchie, M. (2024). Utility of recruitment incentives in early Alzheimer's disease. Alzheimer's Association International Conference. https://alz.confex.com/alz/2024/meetingapp.cgi/Paper/92808
Robbins, R. (2024, January 31). Biogen abandons its controversial Alzheimer's drug Aduhelm. The New York Times. https://www.nytimes.com/2024/01/31/business/biogen-alzheimers-aduhelm.html#:~:text=adviser%20called%20the%20approval%20of,protocol%2C%E2%80%9D%20including%20unusually%20close%20collaboration
Rossiter, J. R. (2019). A critique of prospect theory and framing with particular reference to consumer decisions. Journal of Consumer Behavior: An International Research Review, 18(5), 399-405. https://doi.org/10.1002/cb.1817
Reiman, E. M., Pruzin, J. J., Rios-Romenets, S., Brown, C., Giraldo, M., Acosta-Baena, N., Tobon, C., Hu, N., Chen, Y., Ghisays, V., Enos, J., Goradia, D. D., Lee, W., Luo, J., Malek-Ahmadi, M., Protas, H., Thomas, R. G., Chen, K., Su, Y., Boker, C., Mastroeni, D., Alvarez, S., Quiroz, Y. T., Langbaum, J. B., Sink, K. M., Lopera, F., & Tariot, P. N.; API ADAD Colombia Trial Group. (2023, May). A public resource of baseline data from the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease Trial. Alzheimer's & Dementia, 19(5), 1938-1946. https://doi.org/10.1002/alz.12843
Reiman, E. M., Cummings, J. L., Langbaum, J. B., Mattke, S., & Alexander, R. C. (2024, February). A chance to prevent Alzheimer's disease sooner than you think. Lancet Neurology, 23(2), 144-145. https://doi.org/10.1016/S1474-4422(23)00508-2
Selten, R. (1990). Bounded rationality. Journal of Institutional and Theoretical Economics (JITE) / Zeitschrift für die gesamte Staatswissenschaft, 146(4), 649–658. http://www.jstor.org/stable/40751353
Sexton, C., Snyder, H., Chandrasekaran, L., Worley, S., & Carrillo, M. (2021). Expanding representation of low and middle income countries in global dementia research: Commentary from the Alzheimer's Association. Frontiers in Neurology, 12, 633777. https://doi.org/10.3389/fneur.2021.633777
Solomon, A., Mangialasche, F., Richard, E., Andrieu, S., Bennett, D. A., Breteler, M., Fratiglioni, L., Hooshmand, B., Khachaturian, A. S., Schneider, L. S., Skoog, I., & Kivipelto, M. (2014). Advances in the prevention of Alzheimer's disease and dementia. Journal of Internal Medicine, 275(3), 229-250. https://doi.org/10.1111/joim.12178
Stam, C. J., & de Haan, W. (2024). Network hyperexcitability in early-stage Alzheimer's disease: Evaluation of functional connectivity biomarkers in a computational disease model. Journal of Alzheimer's Disease, 99(4), 1333-1348. https://doi.org/10.3233/JAD-230825
Thaler, R. H., & Sunstein, C. R. (2008). Nudge: Improving decisions about health, wealth, and happiness. Yale University Press.
Wachner, J., Adriaanse, M. A., & De Ridder, D. T. D. (2021). The effect of nudges on autonomy in hypothetical and real-life settings. PLoS ONE, 16(8), e0256124. https://doi.org/10.1371/journal.pone.0256124

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Article

The End of Alzheimer's Disease: Nudging Strategies to Encourage Mass Participation in Clinical Trials

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Abstract: Characterized by amyloid plaques, tau tangles, and neuronal loss, Alzheimer's disease (AD) presents a significant public health challenge, with ever-growing prevalence due to an aging global population. By the time cognitive impairment is detected, the disease's pathology is already extensive and difficult to halt. Despite advances in research and drug development, participation in AD drug trials remains crucial for discovering effective treatments and preventive measures. This article explores how behavioral economics can be employed to raise global awareness about Alzheimer's, motivate individuals to undergo testing, and encourage involvement in experimental drug trials. By integrating nudging strategies with creative educational approaches, this study aims to increase support for AD research.

Keywords: nudging; behavioral economics; Alzheimer's disease

1. Introduction

Every three seconds, someone in the world develops dementia. As of 2020, over 55 million people globally are living with this condition. This figure is expected to nearly double every two decades, projected to reach 78 million by 2030 and 139 million by 2050. A significant portion of this increase will occur in developing countries. Currently, 60% of individuals with progressive cognitive decline reside in low and middle-income nations, a percentage anticipated to rise to 71% by 2050. The most rapid growth in the elderly population is occurring in China, India, and their neighboring countries in South Asia and the Western Pacific (1). Characterized by memory loss and other cognitive impairments, Alzheimer's disease (AD) constitutes the most common cause of irreversible dementia, involving neurodegenerative processes marked by the formation of amyloid plaques and neurofibrillary tangles. Current treatments primarily address symptoms rather than altering disease progression, though research continues into potential disease-modifying therapies, including drugs targeting amyloid and tau proteins. Early diagnosis and intervention are therefore crucial, with ongoing trials focusing on pre-dementia stages like mild cognitive impairment (MCI) to identify effective treatments before significant brain damage occurs (2). This paper combines nudging and other behavioral principles with relevant research and creative strategies in order to emphasize how they can all be applied to increase engagement in Alzheimer's disease research and prevention efforts.

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Unlike cancer, which can sometimes be treated or even miraculously cured, or HIV, which can be managed with proper medication, Alzheimer's disease remains a significant challenge for specialists, presenting difficulties from early symptom recognition to the troubling distinctions between early- and late-onset forms. Since there is still no effective treatment, the medical community continues to grapple with the complex and unforgiving nature of AD in all its manifestations. Nonetheless, this fatal illness, the fifth-leading cause of death among Americans age 65 and older, should not be considered an inevitable part of aging (3). The saying *not all people age in the same way* can therefore be understood in this context as *not all older people get Alzheimer's*. While menopause and andropause represent normal aspects of aging, Alzheimer's does not, although a worryingly large number of elderly individuals believe they are already destined to develop this disease.

A key symptom of Alzheimer's is difficulty remembering recently learned information, as brain cells deteriorate due to the buildup of two problematic proteins: beta-amyloid, in the spaces between nerve cells, and tau, inside them. Other potential causes include head injuries, depression, and hypertension, according to scientists (4). Obtaining an accurate diagnosis at an early age thus proves challenging, as individuals may display different symptoms, depending on whether they are in the early, middle, or late stages of the disease. Comprehensive medical evaluations are therefore required to confirm Alzheimer's, since relying on one or two independent tests can lead to misdiagnosis, which can devastate someone's life.

Over the years, the diagnostic criteria for AD have significantly evolved to focus on presymptomatic and pre-dementia stages, bridging the gap between prevention and treatment trials. One review discusses how improved diagnostic reliability can enhance preventive strategies, the transition from observation to action, and ongoing intervention studies. The paper thus emphasizes the need to understand cognitive impairment and risk factors from a life-course perspective and highlights new approaches such as targeting genetic and beta-amyloid biomarkers, as well as multidomain interventions. International efforts like IDAD and EDPI are therefore key for advancing prevention methodologies and conducting large-scale trials to address AD and dementia globally (5).

Early-onset Alzheimer's disease, also known as younger-onset Alzheimer's, affects individuals in their 30s, 40s, or 50s, adding to the complexity of an already bewildering condition, characterized by plaques and tangles that damage and eventually kill nerve cells. Like the later-onset form, the former has no cure and only offers limited prophylactic treatments, which may be linked to autoimmune diseases such as diabetes or fibromyalgia (6). Thus, one thing is certain: no herb, drug, or regimen can currently cure this deadly disease, so research continues.

2. Behavioral Economics and Nudging

Behavioral economics (BE) explores how psychological factors influence economic decision-making, thereby revealing that individuals often deviate from rational choices due to biases and heuristics. This interdisciplinary field basically combines insights from psychology and economics to understand and predict human behavior more accurately (7).

Health problems are increasingly recognized as behavioral issues rather than purely medical ones, with unhealthy behaviors accounting for a significant portion of premature deaths and poor adherence to long-term therapies. For HIV patients, adherence to antiretroviral therapy (ART) remains suboptimal despite financial incentives, which often prove costly and have only short-term effects. Recent studies, like HPTN065, show limited success with large financial rewards, thus emphasizing the need for alternative approaches. Hence, behavioral economics offers promising insights for improving ART adherence. Instead of relying solely on large financial incentives, BE suggests using small, frequent rewards, non-monetary incentives such as social norms and personal commitments, and effective communication strategies (8). By focusing on how incentives are framed and delivered, and integrating BE principles, researchers can ultimately design more effective and cost-efficient interventions to enhance health behaviors.

Similarly, (9) posits that traditional health incentive programs in U.S. workplaces often fall short because they do not account for the complexities of human behavior. While many programs rely on rational models of education and financial incentives to improve health outcomes, these methods often overlook the irrational ways people make decisions. Asch, too, argues that behavioral economics offers better strategies by understanding psychological biases and creating interventions more aligned with human behavior. For example, framing incentives as losses rather than gains can lead to significantly better outcomes, such as increased physical activity. Asch further suggests that employers can improve health incentives by incorporating behavioral economics principles, which emphasize making changes to how incentives are designed and communicated. Rather than just offering financial rewards, leveraging social incentives and simplifying choices can be more effective. He also points out that health incentives should be tailored to address both general wellness and specific chronic conditions to have a meaningful impact. On the other hand, as seen with testing for HIV or hepatitis, or vaccination campaigns, public response to calls for action might be lukewarm, even with financial incentives. To address this, a combination of financial incentives (compensation or rewards) and recognition incentives (thanking or praising) should be employed to encourage participation, given that recognizing and appreciating individuals' contributions can help foster a positive behavior pattern in populations (10).

In the context of Alzheimer's disease, behavioral economics can be instrumental in designing strategies to increase awareness and participation in drug trials. By applying principles such as nudging, which subtly guides individuals toward more beneficial behaviors without restricting their freedom of choice, researchers and policymakers can effectively motivate people to engage in preventive measures, seek early testing, and contribute to experimental drug studies. This approach can thus leverage behavioral insights to address the complexities of decision-making in health contexts, ultimately improving outcomes in Alzheimer's research and treatment. In other words, by incorporating behavioral economics concepts into the planning and execution of the drug trials, organizers can better address public concerns, motivate participation, and ultimately advance the research efforts against Alzheimer's disease.

(11) introduced the concept of nudging, which draws from social psychology, in order to challenge traditional economic theories that assume individuals always make rational choices to maximize their welfare. Instead, the scholars propose that people often exhibit bounded rationality, which leads to biased decisions that may not align with their best interests. Thaler and Sunstein thus advocate libertarian paternalism, where governments can subtly design choice environments – referred to as choice architecture – so as to guide individuals toward better decisions without removing their freedom of choice. As such, libertarian paternalism seeks to guide individual decision-making by using subtle interventions known as nudges in order to promote welfare-enhancing choices without significantly restricting freedom. Rooted in the law and economics movement, this approach aims to suggest preferable options rather than impose restrictions, thereby preserving personal choice while encouraging beneficial outcomes. Although libertarian paternalism may not serve as an all-encompassing ethical framework, it provides a useful addition to public health ethics by offering a method for gently steering individuals toward better decisions while maintaining their autonomy (12). A nudge is basically defined as any modification in the choice architecture that alters behavior predictably while preserving all options and not significantly changing economic incentives. Nudges can include tactics like adjusting default options, altering how choices are presented, or creating small incentives. The appeal of nudging therefore lies in its simplicity and low cost compared to legislative approaches. For instance, nudging strategies might involve making healthier food options more prominent in canteens or changing the default setting for organ donation to an opt-out system. The approach contrasts with regulatory actions, which might impose stricter measures such as banning smoking in public places or increasing taxes on alcohol and cigarettes (13). As such, the nudge approach presents several benefits for public sector problem-solving, particularly in times of limited resources. The main advantage ultimately lies in its ability to guide individuals toward better choices without imposing direct regulations or significant economic changes, which makes it appealing to governments seeking cost-effective solutions. By subtly influencing the decision-making environment, nudges can thus encourage people to make healthier or more beneficial choices, potentially addressing various public health and behavioral issues (13).

However, the nudge approach also faces criticism for being patronizing and invasive, given that it involves altering people's decision-making environments without their explicit awareness. Critics specifically argue that such methods encroach upon personal autonomy and privacy, their users treating individuals as though they were incapable of making rational decisions on their own. Additionally, there are concerns that nudges might not lead to long-term behavioral changes and could be less effective compared to more direct regulatory measures. For instance, while nudging strategies may lead to modest improvements in salt consumption, they may not achieve the significant reduction seen with comprehensive legislation. The effectiveness of nudging might also be limited if it neglects broader systemic issues such as poverty and inequality, which also influence behavioral patterns (14); (15). Despite these concerns, governments are increasingly adopting nudging techniques in policy-making, as evidenced by initiatives from national Behavioral Insights Teams, which apply behavioral insights to areas like health and consumer behavior (16).

Since the global acknowledgment of libertarian paternalism, researchers have been exploring the effectiveness of nudge and think strategies in encouraging civic behavior and enhancing public service delivery. Their experiments have utilized randomized control trials to assess various interventions, such as feedback on recycling rates and public pledges for charitable donations. For instance, feedback cards improved participation in food waste schemes, and public recognition combined with pledges significantly increased book donations. These findings suggest that nudge strategies can effectively influence behavior through subtle adjustments in the decision-making environment. On the other hand, the think approach, which promotes collective deliberation on controversial issues, also showed promise yet with limitations. Experiments involving online discussions revealed modest shifts in policy preferences and suggested that while online deliberation can engage politically interested individuals, it may not broadly influence the general public. Additionally, mixed results were observed in experiments comparing information versus discussion on organ donation, which indicates that while nudges can prompt immediate actions, they might need to be complemented by broader engagement strategies to achieve sustained behavioral changes (17). Overall, while nudge interventions have demonstrated efficacy in small-scale settings, think approaches highlight the potential for deeper public engagement, although they require more innovative and systemic implementation to be fully effective.

Future research should therefore explore how social interactions and psychological insights can further enhance health outcomes, moving beyond the limitations of traditional economic models. Ultimately, nudging can guide people toward making decisions that align with their best interests, particularly in the context of preventing and curing AD.

3. Research Insights

3.1. High-profile announcements

In 2015, Charlie Sheen publicly revealed that he was HIV positive, a disclosure driven by his frustration with being blackmailed over the secret he had kept for years. So profound and unexpected was the impact of his announcement that it sparked a significant increase in the purchase of at-home HIV testing kits, demonstrating how his candidness had a tremendous effect on public behavior. As one article aptly put it, Sheen's honesty was equivalent to the impact of seven World AIDS Days combined (18).

The case of Charlie Sheen's disclosure of his HIV status demonstrates the power of celebrities' personal announcements in influencing public behavior. Similarly, prominent figures speaking about their experiences with AD or advocating research participation can have a significant impact on public attitudes and engagement.

3.2. FDA Approval Controversies

Several years ago, despite internal disagreement and insufficient evidence of benefit, the FDA approved Biogen's Alzheimer's drug, Aduhelm (aducanumab), under a controversial accelerated approval process. The decision faced significant criticism from experts and led to investigations into the approval process and pricing. A council of fifteen FDA officials had earlier determined that another clinical trial was necessary, warning that premature approval

could lead to widespread use without clear benefit or potential harm. Despite this, the FDA collaborated unusually closely with Biogen, which some argued compromised regulatory integrity, resulting in the approval of a drug that showed minimal efficacy in trials and was associated with risks like brain swelling and bleeding. The approval has sparked widespread backlash, with major medical centers opting not to offer Aduhelm and professional organizations like the American Neurological Association still opposing the approval. The FDA justified the decision by citing the accelerated approval program, which allows drugs targeting serious diseases with few treatment options to be approved based on biomarker effects that are "reasonably likely to predict clinical benefit." This rationale was controversial as many Alzheimer's experts believe there is insufficient evidence linking amyloid plaque reduction, Aduhelm's primary action, to cognitive benefits. The FDA's handling of the approval process, including its close ties with Biogen and deviations from typical procedures, has remained under intense scrutiny ever since (19).

In 2024, Biogen has finally decided to abandon its ownership rights to Aduhelm, the controversial Alzheimer's drug, and discontinue the clinical trial that the FDA had mandated to confirm the drug's efficacy. As the initial approval of Aduhelm was met with fierce criticism due to the weak evidence supporting its benefits, this decision concludes a contentious period marked by outrage over the FDA's approval process, which involved irregularities and close collaboration with Biogen, and concerns about the drug's safety risks, such as brain swelling and bleeding. The financial and practical impacts of Aduhelm have been significant. Initially priced at $56,000 annually, it was expected to be widely used, potentially straining Medicare's budget and generating substantial revenue for Biogen. However, Aduhelm's market performance was dismal, bringing in only $7.8 million in its first year and a half. Medicare's decision to limit coverage to patients in clinical trials further hindered its adoption. Despite Biogen's statement that their withdrawal was not due to concerns over safety or effectiveness, the company's revenue from Aduhelm has been negligible. As Biogen exits from Aduhelm, the rights will revert to Neurimmune, the original licenser. Biogen will continue to supply Aduhelm until its license is withdrawn in November 2024. However, patients in the confirmatory clinical trial will only receive prescriptions for the drug until May. Meanwhile, the Alzheimer's treatment landscape has shifted, with new drugs like Leqembi from Biogen and Eisai, and donanemab from Eli Lilly, showing evidence of slowing cognitive decline, although their effects may not be significantly noticeable to patients (20). This shift indicates a move toward more promising therapies in the battle against Alzheimer's disease.

The controversial approval of Biogen's Aduhelm highlights the complexities and challenges in drug approval processes, which can lead to a decline in trust in the regulatory process. By understanding these dynamics, nudging strategies can be designed to address concerns and build more trust in the research and approval processes. AD research has long acknowledged modifiable risk factors. *The Handbook of Prevention and Alzheimer's Disease* explores this field, known as the AD preventome, which now includes 12 risk factors potentially contributing to 40% of dementia cases globally. This new book educates on these factors and biomarkers, emphasizing their role in enhancing brain health and reducing AD risk while it also covers prevention domains like vascular health, social engagement, sleep, and spirituality (21). Alongside its companion volume on intervention, this recent study provides a comprehensive guide to strategies for preventing and addressing AD, useful for all professionals in the field.

Polygenic risk scores (PRS) are commonly used to predict disease risk by combining genetic markers, but they fail to capture the full heritability of complex diseases like late-onset Alzheimer's disease (LOAD) and lack generalizability across different populations. One significant study aims to improve LOAD risk prediction by developing a paragenic risk score that incorporates epistatic interaction features and machine learning methods. The new model enhances PRS by including interactions between SNP loci through an evolutionary algorithm and by using an ensemble of non-linear machine learning models to estimate risk. Compared to traditional PRS models, the paragenic model demonstrates significantly higher accuracy, achieving an AUC of 83% and matched sensitivity/specificity of 75% under 10-fold cross-validation, and maintains accuracy on independent datasets and within APOE genotype strata (22). This approach shows promise for better predicting disease risk in complex heritable conditions like LOAD.

Unlike LOAD, early-onset Alzheimer's disease (EOAD) proves more heterogeneous, necessitating further exploration of its contributing proteins and pathways. Another very recent study used mass spectrometry to analyze cerebrospinal fluid (CSF) proteomics from a cohort of 139 samples – individuals with normal cognition, EOAD, and LOAD. Through correlation network analysis and machine learning, researchers identified differentially expressed proteins and associated pathways in EOAD, thus quantifying 2,168 CSF proteins and finding EOAD to exhibit more significant protein expression changes and synaptic dysfunction compared to LOAD. Three potential biomarkers for EOAD – SH3BGRL3, LRP8, and LY6H – were thus identified, with SH3BGRL3 accurately classifying EOAD in an additional Western cohort (23). These findings offer a comprehensive CSF proteome profile for EOAD and highlight three promising biomarkers for early diagnosis.

3.3. Genetic Research Initiatives

Specialists remain perplexed by the causes of younger-onset Alzheimer's disease, especially what is now termed familial Alzheimer's disease, caused by rare deterministic genes inherited across multiple generations. This tragic reality affects many families in and around Medellín, the capital of Colombia's Antioquia province, although it also offers hope for a future cure. A particularly large family in Colombia, plagued by the rare genetic mutation E280A, has allowed researchers to study this mutation that predisposes them to Alzheimer's disease by age 45, ultimately leading to premature death. Owing to this research opportunity, Francisco Lopera, a clinical and behavioral neurologist at the University of Antioquia, and Kenneth S. Kosik, a neurologist and professor at the University of California, Santa Barbara, have developed an experimental drug, securing $15 million in grant funding from the National Institutes of Health (NIH) for a major trial. This antibody ultimately aims to clear beta-amyloid and prevent tau protein buildup, thereby preventing neuron death and the formation of deadly plaques and tangles. As a critical part of the project, 300 members of this extended family from Antioquia agreed to start testing the expensive medication several years ago (24). They all carry the E280A mutation in the presenilin 1 gene, which makes them virtually certain to develop early-onset Alzheimer's disease. The participants are aged 30 to 60 and none have shown symptoms at the start of the trial.

The study, known as the Alzheimer's Prevention Initiative (API) Colombia Trial, proves one of the most ambitious and groundbreaking efforts to understand and potentially prevent AD. The drug under investigation is called crenezumab, developed by Genentech, a member of the Roche Group. Crenezumab is an antibody designed to bind to and clear amyloid-beta, a protein that accumulates in the brains of Alzheimer's patients. Participants are randomly assigned to receive either crenezumab or a placebo. The trial is double-blind, meaning neither the participants nor the researchers know who is receiving the actual drug versus the placebo. Participants receive injections every two weeks over a five-year period. The primary goal is to determine whether crenezumab can prevent or delay the onset of cognitive decline and dementia in people who are at genetic risk for Alzheimer's but are currently asymptomatic. Secondary measures include assessing changes in biomarkers related to Alzheimer's, such as amyloid plaques and tau tangles in the brain, through imaging studies and cerebrospinal fluid analyses. Besides NIH, the trial is funded by a combination of sources, including Banner Alzheimer's Institute, Genentech, and other organizations committed to Alzheimer's research (25). The total funding for the project is therefore substantial, with significant contributions aimed at ensuring the trial's comprehensive nature and long duration.

However, the study faces several challenges, including ethical considerations of testing a drug on individuals who are not yet symptomatic but are certain to develop the disease. There is also the challenge of ensuring participant adherence to the trial protocol over the long term and managing the psychological impact of genetic knowledge on participants and their families. As of recent updates, the trial has been progressing, with researchers closely monitoring interim results (26). While complete results are not yet available, there is optimism in the scientific community about the potential findings, as the interim analyses are already helping determine the drug's safety and early efficacy signals. As a specific part of the project, the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease (API ADAD) Trial evaluated the efficacy of the anti-oligomeric amyloid beta antibody therapy crenezumab in cognitively unimpaired members of the Colombian presenilin 1 (PSEN1) E280A kindred.

The study outlines methods to ensure participant confidentiality and anonymity while making baseline data available to researchers. These methods included assessing potential risks, masking identifying variables, and implementing data management safeguards. Researchers can now request access to baseline demographic, genetic, imaging, clinical, and cognitive data, as baseline data are publicly accessible and future access to treatment data and biological samples will adhere to the original trial agreement and principles developed by the Collaboration for Alzheimer's Prevention. This data sharing aims to facilitate the exploration of crucial questions, such as the effects of starting investigational Alzheimer's prevention therapies before and after detectable amyloid plaque deposition (27). This initiative is thus expected to advance Alzheimer's research significantly by making extensive trial data available to the scientific community.

Similarly, network hyperexcitability (NH) is emerging as a key pathophysiological process in early Alzheimer's disease (AD) and a potential treatment target. Functional connectivity (FC) measures have been proposed as biomarkers for NH, but their sensitivity in early-stage AD is unclear. An important study employs a whole brain computational model simulating progressive AD pathology to evaluate the performance of four FC measures: amplitude envelope correlation corrected (AECc), phase lag index (PLI), joint permutation entropy (JPE), and a novel phase lag time (PLT). The model replicates clinical spectral changes and NH progression. Results indicate that JPE and PLT are more sensitive than AECc and PLI in detecting early NH and AD-related abnormalities, suggesting that these novel FC measures could enhance early diagnosis and treatment targeting in AD (28). Furthermore, recent developments suggest a realistic opportunity to develop, gain regulatory approval for, and implement effective preventive therapies in the near future. As such, intravenously administered anti-amyloid antibodies for secondary prevention may be available within three years, with subcutaneous self-administered therapies soon after, and subcutaneous antibody therapies for primary prevention potentially within five years (29).

4. Testing and Drug Trials

The participation of people of different ages in testing crenezumab worldwide will significantly impact the medical field's efforts to stop and prevent Alzheimer's disease, so mass volunteering for drug injections proves crucial. Although such a revolutionary discovery might inspire people aged 30 to 65 to take action against Alzheimer's disease, this shift in consciousness cannot happen overnight or through individual efforts alone, especially when people are still healthy. Also, mass testing over many years will prove costly, necessitating close monitoring of participants globally and international collaboration, with periodic exchanges of results between researchers, along with constant feedback and brainstorming sessions. If future generations understand their pivotal role in combating and eventually eradicating Alzheimer's, the research process initiated with the Colombian family will continue seamlessly. By fostering global awareness and cooperation, the potential for significant advancements in preventing and treating AD will increase, which ensures that the groundbreaking efforts of the initial trial can be built upon and expanded worldwide.

As soon as all the side effects of the test drug have been addressed, the world will be provided with a safer and more effective antibody to prevent the formation of plaques and tangles in the brain, regardless of age. Therefore, the crucial behavioral shift needed is for adults to decide to participate in the mass testing of this experimental Alzheimer's medicine. Each country should establish testing centers in designated hospitals within cities where individuals can receive bi-weekly injections of the drug. These centers should be widely advertised through billboards, commercials, campaigns, and other forms of media, both inside and outside medical institutions, which can be facilitated by a responsible healthcare system working in conjunction with a proactive media industry. Additionally, organizing National Testing Days by Alzheimer's associations worldwide could help inform people about AD and the benefits of participating in drug trials.

In essence, global efforts will focus on raising awareness about the crucial role individuals in helping to cure Alzheimer's by participating in further testing of the experimental drug. However, encouraging people voluntarily to receive injections twice a month, especially when they are asymptomatic, will be challenging. Overcoming fears of potential side effects and the

discomfort of regular injections will require comprehensive education and reassurance about the drug's safety and the importance of mass contribution to medical research.

After mediatized communication of the research results from Colombia, this global initiative could be implemented across all countries simultaneously by using various methods of fostering collective participation in the AD drug testing: informing populations about Alzheimer's disease through leaflets, brochures, commercials, billboards, and similar channels; hosting workshops and seminars on AD and the benefits of drug trials; running constant campaigns against AD and promoting the benefits of drug trials; organizing National Testing Days, where people can meet others with the same disease or potential symptoms; conducting educational sessions in schools and workplaces, or even door-to-door initiatives; establishing support groups for participants in the drug testing to share their experiences; providing counseling and psychological support through NGOs to address issues and fears related to long-term testing; securing endorsements from officials or celebrities with influential authority; holding benefit concerts and other charity events to support testing centers; offering additional services through medical and governmental institutions (30); (31); (32). These efforts aim to ensure widespread awareness and participation in the testing of the experimental Alzheimer's drug, emphasizing the importance of collective action in combating and potentially curing this disease.

A major challenge to this initiative is securing consistent grant funding for each participating country, given that sustaining the collective trial research project over many years requires substantial financial support, which no single health organization or National Institute of Health can provide indefinitely. Moreover, it is unrealistic and unethical to expect less developed countries to contribute financially on par with highly developed nations. To mitigate these challenges, several strategies could be implemented: developed countries and international organizations could pool resources to support less developed countries, thus ensuring equitable participation without financial strain and international disputes; engaging private sector stakeholders to contribute financially and logistically can also supplement public funding; international authorities can develop adaptable funding mechanisms that can be scaled up or down, based on the needs and capabilities of each country; clearly communicating the importance of the clinical trials and the potential long-term benefits can help garner public and governmental support; actively involving community leaders and influencers in promoting the initiative can enhance public trust and participation; rolling out the initiative in phases, starting with pilot programs in select regions worldwide, can help manage resources and demonstrate success before wider implementation (33); (34).

In order to motivate individuals to participate in worldwide testing and experimental drug trials, the following personalized nudging strategies should also be considered: risk communication; simplified access; incentives and reminders. Thus, utilizing tailored communication strategies to convey the importance of early testing and trial participation and highlighting individual risk factors, such as genetic predispositions or lifestyle choices, can make the need for testing more relevant and urgent. Also, making the process of enrolling in trials as easy as possible can certainly remove barriers to participation. For example, streamlining registration procedures and offering trial information through easily accessible platforms can encourage more people to get involved. Additionally, providing small incentives, such as gift cards or public recognition, can motivate participation while using reminders and follow-ups can keep individuals engaged and informed about the trials.

Besides targeted nudging, organizers of large-scale drug trials should particularly consider several other concepts from behavioral economics and science to encourage effective participation and manage public perception:

Attribute Framing – Prospect Theory – Expected Utility (35)

The way drug trials are framed will significantly influence people's decisions. If the benefits and risks of participating are framed positively, emphasizing potential long-term gains and the proactive role in combating Alzheimer's, people may be more inclined to participate. Conversely, framing the trial in terms of risks or uncertainties might deter potential

participants. People's choices are often influenced by their anticipated utility values, which means that they weigh potential gains against potential losses.

Bounded Rationality vs. Rational Decision Making (36)

Acknowledging that individuals often operate under bounded rationality – limited cognitive resources and time – can help in designing the trials' communication strategies. While people may not always maximize their decision-making utility due to these limitations, they tend to use heuristics to make satisfactory decisions rather than optimal ones. Understanding this can help in crafting messages that simplify the decision-making process and make participation more appealing.

Loss Aversion – Risk Aversion – Status Quo (37)

People are generally more motivated by the fear of loss than by the potential for gain. They may therefore prefer to avoid the risk of participating in a drug trial due to fears of potential side effects, even if the trial offers a chance to prevent Alzheimer's disease. This aversion to risk and preference for maintaining the status quo can be addressed by clearly communicating the potential benefits and minimizing perceived risks. Emphasizing the safety measures and monitoring in place can also help alleviate fears.

Two Systems of Thinking (38)

Decision-making about participating in the drug trials will engage both System 1 (intuitive and emotional) and System 2 (deliberative and analytical) thinking. Initially, System 1 might lead to a quick, fearful response due to perceived risks. However, System 2 thinking, which involves more thoughtful consideration, might reveal the benefits and overall importance of the trials. Crafting messages that appeal to both systems can therefore help ensure that the decision to participate is well-informed and considered from both emotional and rational perspectives.

Information Avoidance – Inattention (39)

People may choose to ignore information about Alzheimer's disease or the drug trials due to the belief that it does not concern them since they are currently healthy. To combat this, it is essential to create awareness campaigns that not only inform but also engage individuals on a personal level while indicating how participation could benefit them and others in the long run. Ensuring that information is accessible, relevant, and presented in a way that captures attention can thus overcome this avoidance.

Empathy Gap – Projection Bias – Social Conformity (40)

Individuals often fail to appreciate future risks or benefits until they experience them directly. By highlighting personal stories and testimonials from those affected by AD, nudging can bridge this empathy gap, making the disease's impact more tangible. Also, people tend to underestimate their future risk of disease. Providing information about the growing prevalence of AD and the benefits of early participation in research can make anyone more aware of their potential future risks. As people are most often influenced by others' behavior, nudging can leverage social proof to encourage participation by showcasing high-profile endorsements or involving community leaders in promoting AD awareness.

Endowment and IKEA Effects (41)

Individuals value things more highly if they work with them and perceive them as their own. As such, by involving individuals in educational activities or trial-related events, such as community workshops or local fundraisers, authorities may help entire communities develop a stronger sense of ownership and commitment to AD research.

Thus, by addressing funding challenges and employing a multifaceted approach to incentivize participation, the global initiative could eventually achieve its goal of widespread involvement in Alzheimer's drug testing and research.

5. Increasing Awareness of Alzheimer's Disease

Owing to its potential to prevent, halt, and slow the progression of Alzheimer's disease, the drug crenezumab is currently being tested on perfectly healthy participants in Colombia. Of these, 200 carry the gene defect, while 100 do not. Furthermore, only 100 of the 200 are receiving the test drug every two weeks while the remaining 100 receive placebo injections. Researchers are hopeful that the drug will prevent the disease in those currently taking it, paving the way for further testing on individuals susceptible to Alzheimer's worldwide, both young and old. If completely successful, the drug could be taken preventively by everyone to ensure they never have to contend with this unforgiving disease (24). However, this achievement will require many more years of trials, and larger sample sizes to expedite and improve the results.

While individuals already diagnosed with AD may not require additional motivation to participate in drug trials, healthy people, especially those in their 30s and 40s, will likely need more encouragement. Effective nudging, supported by concepts like the endowment effect (valuing what one already has) and the IKEA effect (placing higher value on things one helps create), can increase participation in drug testing. Family influence is also crucial, so authorities should consider creating a new animation franchise that educates and entertains people of all ages about AD. Cartoons have a broad appeal and can address serious issues in a relaxed and engaging manner, as seen with successful films like *Inside Out*, *The Incredibles*, *Zootopia*, and *Wall-E* (42); (43). Introducing a series like *The Alzhy Family Goes Nuts … or Not* could therefore be a novel approach. This fictional family, comprised of humorous guinea pigs, could represent the extended Colombian family initially involved in drug testing while honoring the animals used in research. Through relatable narratives, the storyline could explore various manifestations of early- and late-onset AD, educating, entertaining, and inspiring action all at once. It can thus provide information about Alzheimer's disease in a way that is accessible and engaging for all ages. Also, it can use humor and relatable characters to draw viewers in and make learning about AD enjoyable. Ultimately, it can motivate people to participate in drug trials by demonstrating the importance of the research and how it affects everyone.

All in all, introducing the name Alzhy /ˈæltsɪ/ in the context of a new animation series could foster a greater understanding of Alzheimer's disease while engaging a broad audience. Each episode could start with this explanation: *Alzhy is short for Alzheimer's disease, a name that honors all those who suffer from or are at risk of this condition*. This recurrent introduction would consequently help embed awareness of AD into viewers' minds at a subconscious level. The creative series, featuring *The Alzhy Family*, would air daily at child-friendly hours, providing a playful yet educational approach to understanding Alzheimer's. The guinea pig characters would navigate various scenarios illustrating AD-related challenges, including healthy living, brain health, symptoms of ad, medication and treatment. The Alzhies will eat healthily and do physical exercises to avoid obesity while undergoing brain tissue examinations and engaging in activities like reading, playing board games, solving puzzles, learning new skills. Some of the characters will still experience memory loss, difficulty walking or speaking, and other symptoms of early- or late-onset AD, and therefore they will take medication and participate in experimental drug trials.

Much like Tom and Jerry or Scrat in *Ice Age*, where characters face exaggerated mishaps in a humorous way, *The Alzhy Family Goes Nuts … or Not* would use humor to address the serious topic of AD. Given its emotional impact, this approach will render complex issues more accessible and engaging while episodes could integrate educational content about treatment and prevention strategies in a format both entertaining and instructive. Capitalizing on the success of the series, merchandise such as mugs, t-shirts, action figures, and shopping bags featuring The Alzhy Family could be developed, which will leverage the endowment and IKEA effects, making people more connected to the franchise through their physical possessions. To maximize the impact, some episodes could emphasize memorable and emotionally powerful moments. This approach aligns with the peak-end rule, which suggests people can

easily remember the most intense moments along with the end, which can influence their overall perception of an experience.

Thus, by integrating these elements into a comprehensive strategy, *The Alzhy Family Goes Nuts … or Not* could effectively use educational media and entertainment to increase awareness and participation in Alzheimer's disease research. The series would not only engage audiences but also foster a greater understanding of AD, motivating more people to contribute to research efforts and support drug trials.

6. School Experiments

For AD testing, schools in each country could use regular independent samples T-tests, which will compare the means for two classes of school children of different ages (data sets) of no more than 30 pupils or students each. The control group will be educated about AD in the classical way, through brochures, leaflets, workshops, seminars, for seven days in a row. The treatment group will watch each day, for a whole week, a different episode of the pilot series *The Alzhy Family Goes Nuts … or Not*. The goal of the study would be to determine if the observed results could be consistent across the entire population of a town or village, or merely random variations. The hypotheses for this comparison are as follows:

Null Hypothesis (H0): μwillingness to go drug testing 1 = μwillingness to go drug testing 2

Alternative Hypothesis (H1): μwillingness to go drug testing 1 ≠ μwillingness to go drug testing 2

To evaluate these hypotheses, school researchers could then calculate the T-score, which represents the ratio between the difference between the two groups and the variability within each group (44Mishra, 2019). A large T-score indicates significant differences between the groups, while a small T-score suggests similarities. If the p-value is less than or equal to 0.05 (5%), the results will be considered statistically significant, meaning they are unlikely to occur by chance. Additionally, the standard deviation (SD) can be calculated to assess the dispersion of data around the mean (μ) and identify any outliers (45Manikandan, 2011). This measure will help researchers understand the variability in participants' responses and make predictions about their behavior in real-world scenarios, such as their responsiveness to mass drug testing initiatives, particularly among young and healthy individuals.

Ultimately, the API ADAD trial in Colombia exemplifies how targeted research in genetically homogeneous populations can advance AD prevention efforts. By emphasizing the importance of participation in clinical studies, nudging can help drive engagement in similar trials globally, providing crucial insights into whether early intervention can alter the course of the disease, not just for those with the genetic mutation but also for the broader population at risk of late-onset Alzheimer's.

7. Conclusions

Alzheimer may be just an ordinary (and even beautiful) surname, but it carries an unfortunate association with a devastating medical condition, which arises from Alois Alzheimer's work in the early 20th century. Though the German psychiatrist and pathologist never intended to stigmatize others wearing it, his surname has become inextricably linked with a disease that claims millions of lives worldwide each year. Recognized as the most common and most feared type of dementia, Alzheimer's disease (AD) is directly linked to progressive cognitive decline and impairment, concentration difficulties, serious behavior problems, and memory loss – symptoms that develop gradually yet not slowly enough to be surpassed by the long-awaited lifesaving treatment. According to research, amyloid plaques, tau tangles, and neuronal loss are the most common causes of irreversible dementia, so early detection and participation in drug trials are critical for advancing research and finding effective treatments.

An extended family in Colombia presents a unique opportunity for researchers to explore the prevention of Alzheimer's disease, particularly due to their high prevalence of early-onset dementia linked to a rare genetic mutation, E280A, which guarantees Alzheimer's by age 45. This rare genetic defect led the affected Colombians to collaborate with local and international researchers, who secured substantial funding for a trial involving 300 family members. The study aims to test whether administering a drug to clear amyloid plaques before symptoms appear can prevent the onset of Alzheimer's. The trial's design aims to leverage the family's genetic homogeneity and their predictable disease onset, making it an ideal setting for testing preventive measures. Participants are split into groups receiving either the drug or a placebo, and will be monitored for many years to assess the drug's long-term effectiveness. The final results could transform Alzheimer's treatment by providing a method to halt or slow disease progression before symptoms develop, thus offering hope not only to those in the trial but also to later-onset Alzheimer's patients worldwide. If completely successful, the study could revolutionize the approach to preventing AD and shift current treatment paradigms.

However, motivating individuals, especially those without current symptoms, to participate in global trials can be challenging. This article discussed how key principles grounded in behavioral economics could effectively increase awareness, encourage testing, and drive participation in experimental drug trials. Thus, in addition to the various behavioral concepts and biases involved in encouraging mass participation in drug trials – such as attribute framing, loss aversion, empathy gap, and social conformity – employing nudging strategies will also increase participation in AD trials. In order to influence decision-making, nudging involves subtly guidance toward desired behavior by altering the environment in which choices are made yet without restricting individuals' freedom of choice.

The concept of nudging thus aims to steer people toward healthier choices without restricting their freedom, as it uses techniques such as changing the presentation of options or altering environments. While nudging is employed to improve public health outcomes – like promoting the reduction of unnecessary antibiotic use or implementing plain cigarette packaging – many debates center on the ethical implications of influencing choices without someone's awareness. Critics still argue that nudging can be controversial due to differing personal values and the complexity of health decisions, such as the trade-offs between medication benefits and side effects. To address these concerns, more transparent and explicit approaches, like shared decision-making and clear nudge strategies, are recommended. Individuals are therefore encouraged to question health recommendations and consider all options to ensure informed choices and balance the benefits and risks in light of personal values and preferences.

Nevertheless, behavioral nudges can offer a powerful toolkit for increasing awareness, encouraging testing, and driving participation in Alzheimer's disease research. For instance, introducing an animation series like *The Alzhy Family Goes Nuts … or Not* can combine education and entertainment, thereby creating engaging and informative media content that can effectively foster understanding of AD. Featuring a fictional family of guinea pigs navigating AD-related challenges, the series can educate viewers of all ages about brain health, symptoms of AD, and the importance of participating in drug trials. This approach leverages humor and relatability, making complex topics accessible and memorable. Moreover, by producing merchandise related to the animation series, such as t-shirts or mugs, viewers could feel a personal connection to the cause, which taps into the endowment and IKEA effects, as people are more likely to support causes in which they feel personally invested.

In the end, by integrating nudging principles with creative educational strategies, stakeholders could enhance public understanding of AD and foster greater involvement in experimental trials. As the prevalence of AD continues to rise, leveraging these behavioral insights can assist in advancing research and developing effective prevention and treatment strategies.

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References

1. ADI. (2024). Dementia statistics. Alzheimer's Disease International. https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/
2. Korolev, I. O. (2014). Alzheimer's disease: A clinical and basic science review. Medical Student Research Journal, 4, 24-33. http://msrj.chm.msu.edu/wp-content/uploads/2014/12/Fall-2014-Alzheimers-Disease.pdf
3. Alzheimer's Association. (2023). 2023 Alzheimer's disease facts and figures. Alzheimer's Association Report, 14 March. https://alz-journals.onlinelibrary.wiley.com/doi/epdf/10.1002/alz.13016
4. National Institute on Aging. (2024, January 19). What happens to the brain in Alzheimer's disease? National Institute on Aging. https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/what-happens-brain-alzheimers-disease
5. Solomon, A., Mangialasche, F., Richard, E., Andrieu, S., Bennett, D. A., Breteler, M., Fratiglioni, L., Hooshmand, B., Khachaturian, A. S., Schneider, L. S., Skoog, I., & Kivipelto, M. (2014). Advances in the prevention of Alzheimer's disease and dementia. Journal of Internal Medicine, 275(3), 229-250. https://doi.org/10.1111/joim.12178
6. Mendez, M. F. (2019). Early-onset Alzheimer's disease and its variants. Continuum (Minneap Minn), 25(1), 34-51. https://doi.org/10.1212/CON.0000000000000687
7. Raj, N. (2024, April). Effects of behavioral economics on decision-making. In Transforming Business Practices in Changing Global Economy. Two-day International Conference organized by the School of Management and Commerce, ITM University Gwalior.
8. Linnemayr, S., & Rice, T. (2016). Insights from behavioral economics to design more effective incentives for improving chronic health behaviors, with an application to adherence to antiretrovirals. Journal of Acquired Immune Deficiency Syndromes, 72(2), e50-e52. https://doi.org/10.1097/QAI.0000000000000972
9. Asch, D. (2016). Less logic, more health: How behavioral economics can improve incentives. Knowledge at Wharton. http://knowledge.wharton.upenn.edu/article/how-behavioral-economics-can-improve-health-incentives/
10. Ritchie, M. (2024). Utility of recruitment incentives in early Alzheimer's disease. Alzheimer's Association International Conference. https://alz.confex.com/alz/2024/meetingapp.cgi/Paper/92808
11. Thaler, R. H., & Sunstein, C. R. (2008). Nudge: Improving decisions about health, wealth, and happiness. Yale University Press.
12. Ménard, J.-F. (2010). A 'nudge' for public health ethics: Libertarian paternalism as a framework for ethical analysis of public health interventions? Public Health Ethics, 3(3), 229-238. https://doi.org/10.1093/phe/phq024
13. Rainford, P., & Tinkler, J. (2011). Designing for nudge effects: How behavior management can ease public sector problems. The London School of Economics and Political Science. http://eprints.lse.ac.uk/37810/1/Designing_for_nudge_effects_%28lsero%29.pdf
14. Keogh, B. (2017, October 11). Should you be 'nudged' into better health without you even knowing? The Conversation. https://theconversation.com/should-you-be-nudged-into-better-health-without-you-even-knowing-84601
15. Wachner, J., Adriaanse, M. A., & De Ridder, D. T. D. (2021). The effect of nudges on autonomy in hypothetical and real-life settings. PLoS ONE, 16(8), e0256124. https://doi.org/10.1371/journal.pone.0256124
16. Murayama, H., Takagi, Y., Tsuda, H., & Kato, Y. (2023). Applying nudge to public health policy: Practical examples and tips for designing nudge interventions. International Journal of Environmental Research and Public Health, 20(5), 3962. https://doi.org/10.3390/ijerph20053962
17. John, P., Cotterill, S., Moseley, A., Richardson, L., Smith, G., Stoker, G., & Wales, C. (2011). Nudge, nudge, think, think: Using experiments to change civic behavior. Bloomsbury Academic. https://doi.org/10.5040/9781849662284
18. Migala, J. (2017, May 18). The Charlie Sheen effect on HIV testing was equivalent to 7 World AIDS Days. Vice. https://tonic.vice.com/en_us/article/wnwkab/the-charlie-sheen-effect-on-hiv-testing-was-equivalent-to-7-world-aids-days
19. Belluck, P., Kaplan, S., & Robbins, R. (2021, July 19). How an unproven Alzheimer's drug got approved. The New York Times. https://www.nytimes.com/2021/07/19/health/alzheimers-drug-aduhelm-fda.html#:~:text=New%20Alzheimer's%20Disease%20Treatment%20Approved,that%20attacks%20the%20disease%20process
20. Robbins, R. (2024, January 31). Biogen abandons its controversial Alzheimer's drug Aduhelm. The New York Times. https://www.nytimes.com/2024/01/31/business/biogen-alzheimers-aduhelm.html#:~:text=adviser%20called%20the%20approval%20of,protocol%2C%E2%80%9D%20including%20unusually%20close%20collaboration
21. Raji, C. A., Leng, Y., Ashford, J. W., & Khalsa, D. S. (2024). Handbook of prevention and Alzheimer's disease. Advances in Alzheimer's Disease, 10. https://www.j-alz.com/
22. Hermes, S., Cady, J., Armentrout, S., O'Connor, J., Holdaway, S. C., Cruchaga, C., Wingo, T., & Greytak, E. M.; Alzheimer's Disease Neuroimaging Initiative. (2024). Epistatic features and machine learning improve Alzheimer's disease risk prediction over polygenic risk scores. Journal of Alzheimer's Disease, 99(4), 1425-1440. https://doi.org/10.3233/JAD-230236
23. Li, D., Xie, Q., Xie, J., Ni, M., Wang, J., Gao, Y., Wang, Y., & Tang, Q. (2024). Cerebrospinal fluid proteomics identifies potential biomarkers for early-onset Alzheimer's disease. Journal of Alzheimer's Disease, 100(1), 261-277. https://doi.org/10.3233/JAD-240022
24. Hayes, K. (2017, July 14). Colombian family offers rare Alzheimer's research opportunity: Unique genetic mutation allows for preventive medicine trial. AARP. https://www.aarp.org/health/brain-health/info-2017/genetic-mutation-prevent-alzheimers-fd.html
25. Reardon, S. (2018, March 27). Pioneering Alzheimer's study in Colombia zeroes in on enigmatic protein. Nature. https://www.nature.com/articles/d41586-018-03848-4
26. API. (2024). The Alzheimer's Prevention Initiative (API) autosomal dominant Alzheimer's disease (ADAD) Colombia trial. Alzheimer's Prevention Initiative. https://alzheimerspreventioninitiative.com/api-studies/adad-colombia-trial/

27. Reiman, E. M., Pruzin, J. J., Rios-Romenets, S., Brown, C., Giraldo, M., Acosta-Baena, N., Tobon, C., Hu, N., Chen, Y., Ghisays, V., Enos, J., Goradia, D. D., Lee, W., Luo, J., Malek-Ahmadi, M., Protas, H., Thomas, R. G., Chen, K., Su, Y., Boker, C., Mastroeni, D., Alvarez, S., Quiroz, Y. T., Langbaum, J. B., Sink, K. M., Lopera, F., & Tariot, P. N.; API ADAD Colombia Trial Group. (2023, May). A public resource of baseline data from the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease Trial. Alzheimer's & Dementia, 19(5), 1938-1946. https://doi.org/10.1002/alz.12843
28. Stam, C. J., & de Haan, W. (2024). Network hyperexcitability in early-stage Alzheimer's disease: Evaluation of functional connectivity biomarkers in a computational disease model. Journal of Alzheimer's Disease, 99(4), 1333-1348. https://doi.org/10.3233/JAD-230825
29. Reiman, E. M., Cummings, J. L., Langbaum, J. B., Mattke, S., & Alexander, R. C. (2024, February). A chance to prevent Alzheimer's disease sooner than you think. Lancet Neurology, 23(2), 144-145. https://doi.org/10.1016/S1474-4422(23)00508-2
30. Parra, M. A., Butler, S., McGeown, W. J., Brown Nicholls, L. A., & Robertson, D. J. (2019, December). Globalizing strategies to meet global challenges: The case of ageing and dementia. Journal of Global Health, 9(2), 020310. https://doi.org/10.7189/jogh.09.020310
31. Sexton, C., Snyder, H., Chandrasekaran, L., Worley, S., & Carrillo, M. (2021). Expanding representation of low and middle income countries in global dementia research: Commentary from the Alzheimer's Association. Frontiers in Neurology, 12, 633777. https://doi.org/10.3389/fneur.2021.633777
32. Llibre-Guerra, J. J., Heavener, A., Brucki, S. M. D., Marante, J. P. D., Pintado-Caipa, M., Chen, Y., Behrens, M. I., Hardi, A., Admirall-Sanchez, A., Akinyemi, R., Alladi, S., Dorsman, K. A., Rodriguez-Salgado, A. M., Solorzano, J., & Babulal, G. M.; Diversity and Disparity Professional Interest Area Increasing Sustained Diversity in Clinical Trials Working Group. (2023, July). A call for clinical trial globalization in Alzheimer's disease and related dementia. Alzheimer's & Dementia, 19(7), 3210-3221. https://doi.org/10.1002/alz.12995
33. Cummings, J. (2019). The role of biomarkers in Alzheimer's disease drug development. Advances in Experimental Medicine and Biology, 1118, 29-61. https://doi.org/10.1007/978-3-030-05542-4_2
34. ASPE. (2024, April 22). National plan to address Alzheimer's disease: 2023 update. Office of the Assistant Secretary for Planning and Evaluation. https://aspe.hhs.gov/reports/national-plan-2023-update
35. Rossiter, J. R. (2019). A critique of prospect theory and framing with particular reference to consumer decisions. Journal of Consumer Behavior: An International Research Review, 18(5), 399-405. https://doi.org/10.1002/cb.1817
36. Selten, R. (1990). Bounded rationality. Journal of Institutional and Theoretical Economics (JITE) / Zeitschrift für die gesamte Staatswissenschaft, 146(4), 649–658. http://www.jstor.org/stable/40751353
37. Kahneman, D., Knetsch, J. L., & Thaler, R. H. (1991). Anomalies: The endowment effect, loss aversion, and status quo bias. Journal of Economic Perspectives, 5(1), 193-206.
38. Kahneman, D. (2013). Thinking, fast and slow. Farrar, Straus and Giroux.
39. Golman, R., Hagmann, D., & Loewenstein, G. (2017). Information avoidance. Journal of Economic Literature, 55(1), 96-135. https://doi.org/10.1257/jel.20151245
40. HE. (2024). Heuristic Encyclopedia: Find everything you wanted to know about a heuristic. Newristics. https://newristics.com/heuristics-biases/empathy-gap
41. Norton, M. I., Mochon, D., & Ariely, D. (2012). The IKEA effect: When labor leads to love. Journal of Consumer Psychology, 22(3), 453-460.
42. Bedekar, M., & Joshi, P. (2020). Cartoon films and their impact on children's mentality. International Journal of Multidisciplinary, 5(6), 13-18. https://doi.org/10.31305/rrijm.2020.v05.i06.003
43. Chakravorty, D., & Tilak, G. (2021). Socio-cultural effects of visual representation through animated films with special reference to movies Inside Out & Zootopia. International Journal of Future Generation Communication and Networking, 14(1), 2636-2642.
44. Mishra, P., Singh, U., Pandey, C. M., Mishra, P., & Pandey, G. (2019). Application of student's t-test, analysis of variance, and covariance. Annals of Cardiac Anaesthesia, 22(4), 407-411. https://doi.org/10.4103/aca.ACA_94_19
45. Manikandan, S. (2011). Measures of dispersion. Journal of Pharmacology & Pharmacotherapeutics, 2(4), 315-316. https://doi.org/10.4103/0976-500X.85931