A Comparative Expected Value Analysis Study to Determine If the Economic Benefits of the Most Commonly Prescribed Prescription and Non-Prescription Drugs in the United States Provide Economic Value

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ABSTRACT: It was found that anti-biotics, aspirin, bisphosphonates, blood pressure lowering medications, statins, medications treating depression, diabetes, sexual dysfunction and the poly-pill provided economic value, while medications to treat Alzheimer’s, cancer, multiple sclerosis and Clopidogrel were not found to have provided economic value. The current evidence is insufficient to determine if weight loss medication provides economic value or not.

KEYWORDS: Economic value, anti-biotics, aspirin, bisphosphonates, blood pressure, statins, diabetes, sexual dysfunction, poly-pill, Alzheimer’s, cancer, multiple sclerosis, Clopidogrel, weight-loss.

I. INTRODUCTION
In the United States, the total amount of money spent on medications was approximately 511 billion dollars in 2019. Spending increased each year between 2012 and 2019, rising by a total of almost 200 billion dollars during that seven-year period. Brand name drugs accounted for 80 percent of the total medicine sales in 2019 (Mikulic, 2020). Almost one in two people in the United States (or 46% of the population) used one or more prescription drugs in the last month between the years 2015–2016 (Pesce, 2019). It is estimated that in 2019, 4.38 billion prescriptions will be filled throughout the United States at retail pharmacies. By 2025, that number will go up to 4.98 billion, an increase of almost 14 percent (Statista, 2021). From 2019 to 2020, pharmaceutical expenditures grew by 4.9 percent and utilization increased by 2.9 percent. The top drugs in 2020 were Adalimumab (reduces joint swelling), apixaban (prevents strokes), and insulin glargine (long-acting insulin). The study predicts specialty and cancer drugs will drive future spending increases. It was predicted that in 2021 prescription drug spending would increase by four to six percent (Tichy, 2021). The median out-of-pocket cost for adults is $177 and older people pay $456 on average (AMA, 2020). The drug prices in the United States are 256 percent higher compared to other countries (McGrail, 2021). Retail prescription drugs account for 10 percent of total National Health Expenditures in the United States. However, including pharmaceuticals consumed in other health care settings or in hospitals pushes the United States drug spending as a share of NHE, to 17 percent (DHHS, 2016).

A comparative expected value analysis study is a straight forward method to determine the financial viability of investing healthcare dollars in prescription drugs for a range of illnesses or disorders. This approach can be utilized to analyse the likelihood that identified prescription drugs will result in a cost reduction or savings that exceeds the cost to purchase the prescription drugs.

II. RESULTS
Alzheimer’s - None of the pharmacologic treatments (medications) available today for Alzheimer’s dementia slow or stop the damage and destruction of neurons that cause Alzheimer’s symptoms and make the disease fatal (Alzheimer’s Association, 2020). Antipsychotics may be prescribed to treat hallucinations, aggression and agitation.
pharmacologic treatment for agitation and aggression in people with Alzheimer's dementia concluded that non-pharmacologic interventions seemed to be more effective than pharmacologic interventions for reducing aggression and agitation (Watt et al, 2019).

Exercise has a positive effect on overall cognitive function and may slow the rate of cognitive decline in people with Alzheimer's dementia (Farina, 2014). Cognitive stimulation does have beneficial effects on cognitive function and some aspects of well being in people with Alzheimer's dementia (Aguirre et al, 2013). The World Health Organization (2019) strongly recommends physical activity, quitting smoking, and managing hypertension and diabetes to reduce the risk of cognitive decline and dementia. Physical activity appears to be effective in reducing risk (Ogino et al, 2019). In addition to physical activity, emerging evidence suggests that consuming a heart healthy diet may be associated with reduced dementia risk (Barberger-Gateau, 2007). A systematic review of the use of supplements, including (but not limited to) vitamins C, D and E, omega 3 fatty acids, and ginkgo biloba, found little to no benefit in preventing cognitive decline, MCI or Alzheimer's dementia (Butler et al, 2018).

**Antibiotics** - The value of antibiotics priced at around $10 is highly favorable in terms of value when compared with many other interventions. Antibiotics to treat (full cure) a life-threatening or limb-threatening pathogen usually cost between $2,000 and $3,000 (McKellar et al, 2014). More than 150 million prescriptions are written for antibiotics in the United States each year and bacteria are starting to adapt to the drugs and are becoming harder to kill (WebMD, 2020). The economic burden of antibiotic resistance costs the United States up to $20 billion directly, and up to $35 billion indirect each year (CDC, 2013), which comes at a per person cost of around $133 ($20 billion / 150 million prescriptions). At least 30 percent of antibiotics prescribed in the United States are unnecessary, according to new data published today in the Journal of the American Medical Association (JAMA) by the Centers for Disease Control and Prevention (CDC), in collaboration with Pew Charitable Trusts and other public health and medical experts (CDC, 2016). Even though a third of the antibiotic prescriptions are unnecessary they still provide value since it only reduces the overall cost effectiveness and doesn’t eliminate it.

**Aspirin** - One heart attack or stroke will be avoided for every fifty people with heart disease taking aspirin (Stafford, 2017). Aspirin combined with blood pressure medication further reduces the risk of a stroke by preventing blood platelets from forming a clot and provide additional economic value. The cost of a stroke ranged from $20,396 ± $23,256 (Wang et al, 2014) and the expected cost to reduce a stroke was $2,500 ($50 / .02).

**Bisphosphonates** - One hundred post-menopausal women would have to take bisphosphonates in order to avoid a single hip fracture (1%) per year (Wells et al, 2008). The overall rate of non-vertebral fracture was 6 percent in the bisphosphonate group and 9.6 percent in the placebo group (Byun, et al, 2017). Generic Fosamax costs roughly $100 to $200 per year, which would place the cost of preventing a hip fracture at $15,000 ($150 / 1%). According to MD Save, the average cost for a hip replacement in the United States is around $32,000, which would provide a net benefit of $17,000 ($32,000 - $15,000). A pharma-economic model based on individual long-term risks of fracture improves the selection of postmenopausal women for cost-effective treatment with bisphosphonates (van Staa et al, 2007).

**Blood Pressure** – Blood pressure medicines designed to reduce the risk of heart disease, heart attack and stroke cost around $50 per year (CDC, 2020). According to the Agency for Healthcare Research and Quality (Steiner et al, 2012), the average length of hospitalization and related costs for heart attack patients is 5.3 days at $21,500 per stay. Therefore, just one heart attack for every 430 ($21,500 / $50) patients taking blood pressure medication would need to be averted in order for the medication to provide economic value. However, it should be realized that some patients with mildly elevated blood pressure may not benefit from taking blood pressure-lowering medications since these medications can lower a patient’s blood pressure too much, causing falls and other preventable accidents.

**Cancer** - Cancer drugs account for approximately 10 percent of the total prescription drug market (Quintiles IMS Institute, 2017) and new cancer treatments are now routinely priced at more than $100,000 per year of treatment (Light et al, 2013). The list price for drugs affects cost-effectiveness calculations. Using the list price of cancer drugs invariably makes newer drugs appear less valuable, even though health insurers frequently pay prices well below the list price of oncology drugs (Polite et al, 2014). Drugs for which the incremental costs per quality adjusted life year (QALY) gained exceed a certain threshold, often $100,000 per QALY, are deemed to be of low value (Fonseca et al, 2018). Investigators estimate that 9 in every 10 drugs fail at some point in the research and development process (DiMasi, 2013) resulting with estimated costs of drug development (including failed therapies) of over $2 billion per marketed drug (DiMasi 2003). Critics of this view, point to the fact that many marketed therapies received large, initial support from federal sources such as the National Institutes of Health (Kesselheim et al, 2015). It was also pointed out that the pharmaceutical industry spends more on marketing than research and development earns profits in excess of other industries (Anderson, 2014) and that two-
thirds of drugs brought to market have a net present value of returns (lifetime sales) below the cost of development (DiMasi et al, 2003). Reductions in drug prices will lead to reductions in innovation (Scherer, 2004). Lower prices may increase access to cancer therapies, improve cancer outcomes, and possibly lower cancer spending today, but may reduce access to innovative therapies and the possibility of better cancer outcomes moving forward (Acemoglu, 2004). Despite the United States outspending other developed nations, outcomes in terms of preventable deaths and years of life lost to malignant disease were not better and in some cases were significantly worse (Cylus, 2007). In 2005, lower Medicare part B reimbursement for chemotherapy resulted in a dramatic drop in usage after the January 2005 payment change (Jacobson et al, 2010).

**Cholesterol (Statins)** – United States National survey data suggest statin therapy reduced low-density lipoprotein levels by 18.8 percent, which results in 40,000 fewer deaths, 60,000 fewer hospitalizations for heart attacks and 22,000 fewer hospitalizations for strokes in 2008 (Grabowski, 2012). Statin therapy was also associated with a 27 percent reduction in cardiovascular healthcare costs per patient versus placebo (Gotto et al, 2000). An analysis of analysis of 18 trials, including 56,934 patients primarily without cardiovascular disease, demonstrated statins conferred a relative risk reduction (RRR) in all-cause mortality by 14 percent and in stroke by 22 percent (Cochrane, 2013). From 1987 to 2008, the estimated aggregate social value of statins was estimated to be $1,252 trillion that cost an estimated 947.4 billion dollars ($60 per month) or $180 (treatment program spread over three months would cost around $1,200, which is about 24 times the annual cost for generic antidepressant medication. Pfeiffer, Heisler, Piette, Rogers and Valenstein (2010) reported no significant difference in depression outcomes between those randomized in a peer support intervention versus cognitive therapy. The cost to join a weekly support group can cost as little as $15 per week ($60 per month) or $180 (three months). Goyal (2014) reported that mindfulness meditation may be just as effective as medication when it comes to the treatment of depression, and no third-party cost is associated with engaging in mindfulness. Likewise, exercise enhances the action of endorphins circulating throughout the body improving natural immunity and is as effective as reducing mild depression as antidepressant medications (Harvard Health Letter, 2013). The amount spent to treat depressive disorders in the United States is $71 billion (Dieleman, Baral & Birger, 2016), and 16.2 million adults in the United States have at least one major depressive episode in a given year (Koskie, 2018). Therefore, the cost per person (CPP) for depressive disorders in the United States is $4,382 per person ($71 billion / 16.2 million). It was found that exercise and meditation which cost nothing provided the most value treating mild depression followed by medication, which had an annual payback period (APP) of .05.

Diabetes – The age–gender weighted average of the lifetime medical costs for treating type 3 diabetes and diabetes complications was $85,200, of which 53% was due to treating diabetic complications (Zhou, 2013). A decreased A1C of 1% or more was associated with lower total healthcare costs ($685-$950 less per year) than those without an improvement in the A1C value (Wagner, et al, 2001). There are no pharmacologic treatments (medication) that are available that been proven to stop or cure Diabetes, but with the right medication the disease can be controlled (American Diabetes Association, 2018). It costs about $740 a year to keep the disease under control (Nguyen et al, 2020). The most effective treatment to reduce costs would be exercise, diet and insulin therapy. Exercise has a positive effect on the overall treatment and has shown an increase to the overall body health when diagnosed with diabetes as the healthier you are it becomes easier to manage your disease, monitoring your blood sugar does have a beneficial effect on the wellbeing in people with diabetes (Mayo Clinic 2021). Exercise has a positive effect on the overall treatment and has shown an increase to the overall body health when diagnosed with diabetes as the healthier you are it becomes easier to manage your disease, monitoring your blood sugar does have a beneficial effect on the well-being in people with diabetes (WebMD, 2019). In addition, to physical activity adding a healthy diet can be helpful as well (Nall, 2020). Physical activity is effective in increasing the body’s sensitivity to insulin, which helps control the blood sugar elevations (Stoppler, 2020). The combined impact of diet and exercise provide more value since they are deemed to be more effective than medication alone.

| Programs | SR | Cost | Cost/SR | CPP | BPP | AP |
|----------|----|------|---------|-----|-----|----|
| Exercise | 20% | $0   | $0      | $4,38 | $438 | .00 |
| Meditiation | 20% | $0   | $0      | $4,38 | $438 | .00 |
| Medication | 20% | $48  | $240    | $4,38 | $414 | .05 |
| Therapy  | 20% | $120 | $6,000  | $4,38 | $138 | 1.37 |
**Multiple Sclerosis** - Cost-effectiveness thresholds for most drugs treating multiple sclerosis substantially exceeded the commonly accepted $100,000-$150,000 per quality adjusted life year threshold, even when using prices that account for typical discounts and rebates that may apply in real-world practice (ICER, 2017). ICER’s analyses found that the prices of a majority of the drugs reviewed would need to be discounted anywhere from 25 percent to 94 percent, depending on the drug, in order to meet commonly accepted thresholds for cost-effectiveness (ICER, 2017).

**Clopidogrel** - Clopidogrel is a blood thinner that helps in preventing strokes, heart attacks and other heart diseases and has a success rate of 20 percent (Harvard, 2014). It can be given to people who have Acute Coronary Syndrome (ACS); have Peripheral Artery Disease (PAD) and have had a heart attack or stroke in the past (Davydovskaya & Slowiczek, 2019). The cost of this brand name prescription drug is an average of $61.28 (Goodrx, 2021). The average price of an oral tablet of 75 mg is $160 per 15 tablets on Drugs.com (2021). Being a blood thinner there are common side effects of this tablet, like easy bleeding, stomach ache, diarrhea and constipation. The duration and the strength of the dose are decided by the doctor upon examination of the disease and its type. Clopidogrel is also an antplatelet drug, which means that if one is aware of being allergic to such kinds of drugs then they need to make sure to tell their doctor (WebMD, 2020). Even though Clopidogrel is a commonly prescribed disease it is not cost-effective. A recent study journal has proved that generic Clopidogrel is much more cost effective than Clopidogrel. Using the generic version would help reduce healthcare costs to a point (Ko et al., 2018). Through the method of clinical trials and registries their results have shown that a 300 mg dose (administered) is effective in treating ACS (acute coronary syndrome) (Zuzana & Kala, 2008).

**Poly-Pill** - A daily “poly-pill” consisting of three antihypertensive drugs, a statin, and aspirin to prevent cardiovascular disease was found to reduce the lifetime risk of cardiovascular disease by 15 percent in women and by 21 percent in men if the poly-pill were used by people with a risk of cardiovascular disease equal to or greater than 15 percent over ten years. Attaining this goal would require treating 26 percent of the population at a cost of $34–$36 per quality-adjusted life-year. Offering the poly-pill to women at high risk and to men age fifty-five or older would be the best approach and would yield acceptable incremental cost-effectiveness ratios. The poly-pill would be very cost-effective even in the country with the lowest gross national income in our study. However, policy makers must weigh the value of intervention with the polypill against other interventions, as well as their country’s willingness and ability to pay for the intervention (Bautista, et al, 2013).

**Sexual Dysfunction** - Generic, sildenafil can cost as little as $4 per tablet with GoodRx.com. The act of sex is free since legally one can’t charge for it and there is evidence that sex improves one’s health. Men burned an average of 4 calories a minute during sex sessions and women burned 3 calories during sex sessions, which can be more fun than running on a treadmill. Men who had sex twice weekly or more had less risk of cardiovascular diseases, like stroke or heart attack, than those who had sex once a month or less (Hall, 2010). Sex boosts the immune system, burns calories, lowers blood pressure, lessens risk of heart attack, may ward off prostate cancer, relaxes, reduces pain and prolongs life (Castleman, 2021).

**Weight Loss** - The National Center for Health Statistics estimated in 2015–2016 in the United States, 39.8 percent of adults aged 20 and over were obese (including 7.6% with severe obesity) and that another 31.8 percent were overweight (Fryar, 2018). Approximately $147 billion is added medical expenses per year due to obesity in the United States. Therefore, the cost per person (CPP) for one that is obese or the savings in medical expenses would be $1,429 per year (Antonelli, Maalouf, Pearle & Lotan, 2014). It was found that medication provided the most value reducing the prevalence of obesity with an annual payback (APB) of 3.3 years. The American Society of Plastic Surgeons (2019) reported that the average cost for liposuction in 2014 was $3,518. After liposuction, weight gain was reported in 43% (57% success rate) of the responders, 79.7 percent would have the procedure again and 86 percent would recommend the procedure to family or friends (Broughton, Horton, Lipschitz, Kenkel, Brown and Rohrich, 2006). Two weekly personal training sessions would cost $400 per month or $4,800 annually. Those that work with a trainer can expect on average to lose one to two pounds a week and see noticeable results within the first three to six weeks (Arroyo, 2017). McClaran (2003) found that a personal trainer significantly increased clients’ physical activity and 60 percent of study participants were successful. The average cost of Lap-Band surgery is about $3,500 with insurance and $15,000 without insurance (Quinlan, 2019). After 16 years, 62 percent of the 3,227 individuals treated with a laparoscopic adjustable gastric band still had significant weight loss (O’Brien, MacDonald, Anderson, Brennan & Brown, 2013). All prescription weight-loss drugs approved for long-term use produce significant weight loss compared to the placebo (Mayo Clinic, 2018). Studies show that the addition of weight-loss medication to lifestyle changes results in greater weight loss than lifestyle changes alone produce. Over the course of 12 months, one can expect a mean weight loss of 3 to 7 percent of total body weight beyond that achieved with lifestyle changes alone (Mayo Clinic, 2018). Phentermine (Adipex-P) is a popular drug used to decrease appetite that is available in a generic version (Mayo Clinic, 2018). On-line retailers selling the
Adipex-P quote an average retail price of $34.33 with an annual cost of $411.96. After stopping weight-loss medication people often gain back some of the weight they lost. However, adopting healthy lifestyle habits may help limit weight gain. The ten-year cost would be $4,119.60. Phentermine based on 524 user ratings, was found to be 87 percent effective (Drugs.com, 2019).

| Program  | SR | Cost | Cost/SR | CPP | BPP | CPP/  |
|----------|----|------|---------|-----|-----|-------|
| Drugs    | 87%| $4,110| $4,724  | $1,42| 9   | - $3,29 |
| Liposuction | 57%| $3,518| $6,172  | $1,42| 9   | - $4,74 |
| Trainer  | 60%| $4,800| $8,000  | $1,42| 9   | - $6,57 |
| Lap Band | 62%| $15,000| $24,193 | $1,42| 9   | - $2276 |

There is currently not a consensus on whether or not a 3.3 year payback period for weight loss drugs provides economic value or not.

**SUMMARY**

A comparative expected value analysis study was used to determine if the healthcare dollars invested in the most commonly used prescription results in a net cost savings. The amount of data available for each condition varied significantly. However, the analysis provides a clear snapshot of the likely cost to treat disease with prescription drugs.

It was found that anti-biotics, aspirin, bisphosphonates, blood pressure lowering medications, statins, medications treating depression, diabetes, sexual dysfunction and the poly-pill provided economic value, while medications to treat Alzheimer’s, cancer, multiple sclerosis and Clopidogrel were not found to have provided economic value. However, generic Clopidogrel was found to have provided value. The current evidence is insufficient to determine if weight loss medication provides economic value or not. Currently, none of the medications prescribed to slow or stop the damage and destruction of neurons that cause Alzheimer’s symptoms and make the disease fatal provide value (Alzheimer’s Association, 2020).

**CONCLUSION**

The results of this study may potentially impact a variety of stakeholders who stand to benefit from the findings. A primary group would be individual patients who make decisions to undergo early screening and treatment based on financial considerations. Private insurance companies and hospitals constitute another group of stakeholders as they are major players on the supply side. The cost effectiveness of these services is a major factor in determining the extent of their availability. It’s important to note that politicians who deliberate public policy formulation regarding national healthcare issues would be another important category of stakeholders. The Congressional Budget Office uses the comparative expected value approach to determine the cost effectiveness of prescription drugs as they develop healthcare policy. The methodology employed in this study is in line with those employed in similar studies within the literature.

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