The Counter-productive Problem of Overmedication in the United States

Gupta, Ansh

Michael A. Evans Center for Health Sciences, Marian University, Indianapolis
3200 Cold Spring Rd, Indianapolis, IN 46222

Introduction

What is Overmedication?
Overmedication is a very broad term with many definitions, each centering around the concept of administering too much medication(s). Though not to the point where it may be considered an overdose, it is still considered excessive/unnecessary and can lead to side-effects. In the context of this presentation, I will be referring to the more specific definition of "**over-prescription**," – the concept that a patient is prescribed more medication than is necessary to resolve their condition.

Top 5 most overused medications in the US
To better understand the problem of overmedication, it may help to focus on some of the top ten most prescribed drug classes in the US. A study in the National Library of Medicine (NLM) focused on drug classes which may warrant closer analyses on their benefits vs. side-effects. It was identified that Proton Pump Inhibitors (PPIs) for indigestion, Levothyroxine for hypothyroidism, Statins, Opioids for chronic pain, and Antidepressants were some of the most frequently prescribed drugs [1].

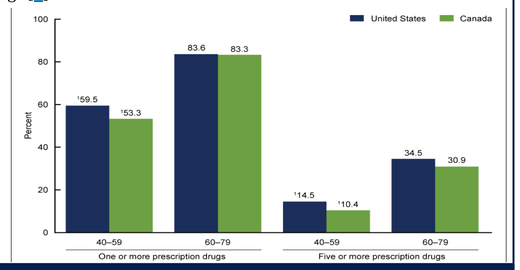

Figure 1: Use of prescription drugs over a 30-day period in 2015-2016 in the US and Canada [2].

Levothyroxine

What is Levothyroxine?
Levothyroxine is the primary medication for treatment of primary, secondary, and tertiary hypothyroidism. It works as a synthetic version of the naturally produced thyroid hormone: thyroxine (T4). Natural thyroxine plays a significant role in directly influencing body metabolism. Levothyroxine mimics this role in the absence of sufficient natural T4 [12].

Long-Term Treatment Concerns
Levothyroxine is known to have some adverse effects which are usually due to **dosing errors** or allergies. Its contraindications are **renal system** and **cardiovascular-related (MIs, myocarditis, cardiac arrythmias)**. There have been some studies attempting to link long-term Levothyroxine to cancers, but there has not been any inclusive evidence to date [13,14,15].

Overprescription
Overprescription problems begin with the treatment of **subclinical hypothyroidism**, a diagnosis of mildly elevated TSH in the presence of normal thyroxine. Studies suggest that 90% of levothyroxine prescriptions are improper because they are used to treat mild subclinical hypothyroidism or even normal thyroid function, leading to minimal improvement in quality of life. One study found that ~23 million in the US are prescribed Levothyroxine – however, ~21 million likely don't need it due to **diagnosis errors** [19]. A study from the *Journal of the Endocrine Society* discussed the effects of **shifting seasons** on the variance of thyroid function in Japanese populations. This study found that TSH peaked in winter months while dipping in the summer [17]. This suggests the possibility of many hypothyroidism misdiagnoses – highly alarming when considering adverse effects such as anxiety, diarrhea, and in the worst cases: cardiovascular morbidities and death [18].

Proton Pump Inhibitors

What are Proton Pump Inhibitors (PPIs)?
Proton Pump Inhibitors (PPIs) are a class of drugs which focus on stomach acid production and a variety of diseases/disorders related to it. PPIs typically function to decrease the production of stomach acid. Their mechanism of action (MOA) focuses on the downstream inhibition of neurotransmitters acetylcholine, histamine, and gastrin (all of which regulate H^+ ion production). They are used as first-line therapeutic agents for GERD diseases such as NERD, esophagitis, Peptic ulcer disease, Zollinger-Ellison syndrome, etc. [4].

Long-Term Treatment Concerns & Overprescription
One study from 2008 found that 25-70% of patients worldwide take PPIs without proper indication. The same study found that it is common for patients to be prescribed PPIs during an impatient stay to prevent stress ulcers and gastrointestinal bleeding. Following discharge, many patients continue taking their PPIs without indication or planned date for cessation [11].
Many studies have been conducted focusing on the long-term adverse effects of PPIs. Initially, these adverse effects were limited to calcium malabsorption, Vitamin B_{12} deficiency, and in recent years, long-term PPI usage has been linked to dementia and chronic kidney disease (CKD). A few of these will be focused on below:

- **Calcium** is essential to bone health and is primarily derived from the diet and oral supplements. When stomach pH is too high (due to PPI usage), calcium is not absorbed into the blood and is eliminated with waste products. A 2012 survey focused on hip fracture rates in women taking PPIs. The study found a 35% increase in hip fracture rate in women taking PPIs for at least 2 years. The risk was higher in women who took PPIs for longer periods. Finally, women who stopped using PPIs for >2 years had a hip fracture risk comparable to those who never took PPIs [10].
- **Vitamin B_{12}** has been determined to be essential for proper cognitive function. Like calcium, Vitamin B_{12} requires a more acidic environment for proper absorption. Data has demonstrated that patients presenting with cognitive decline have been found to have improper myelination lesions – specific to B_{12} deficiency. This link of B_{12} deficiency to cognitive decline has led to the hypothesis of **Dementia** development due to excessive PPI usage. In a 2016 study, researchers found patients aged >75 who used PPIs regularly (at least one prescription every 3 months) had a 44% increased risk of dementia incidence [9].
- **CKD** has been estimated to afflict more than 10% of the population in the US. Many studies have found links between PPI usage and acute interstitial nephritis (AIN) and acute kidney injury (AKI) [7,8]. A study using a long-term running cohort found that patients who regularly used PPIs had an increased risk of CKD at 145% and an increased risk of AKI at 172%. Increased dosage found an increased risk of CKD [6].

Statins

What are Statins?
Statins are used for the treatment of a multitude of types of hypercholesterolemia, hyperlipoproteinemia, and hyperglyceridemia. They work to decrease overall cholesterol, specifically lowering LDL while simultaneously raising HDL. Statin have a complicated MOA, but to summarize they focus on the inhibition of HMG-CoA reductase, an enzyme critical for cholesterol synthesis [16].

The Statin Controversy
Statin's have widely been regarded as the "golden standard" for cardiovascular disease (CVD) prevention. However, there is still controversy regarding their overprescription – especially statin use as **primary preventatives**. One study in the BMJ showed no benefit in individuals with a 10-year CVD risk of <20% [21]. This revelation begs to question: Why are so many patients in this risk range still prescribed statins and what are the potential adverse effects? Unfortunately, most studies on statins have been based on **industry-based trials** aimed at the benefits. These trials tend to exclude large numbers of participants after screening, as revealed from a study by the Heart Protection Study which excluded ~36% of its participants, many of whom may suffer from adverse effects due to statins, before the trial began. Other, **community-based studies** suggest that more than 60% of patients struggle with compliance with statins due to adverse effects [22]. These studies not only bring into question the credibility of industry studies focused on statin benefits in low-risk groups, but also the bigger problem behind this controversy.

Antidepressants

What are Antidepressants?
Antidepressants are a broad class of drugs used to treat not only depression, but a variety of medical disorders such as obsessive-compulsive disorder (OCD), generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD). The MOAs of these drugs typically work to increase concentrations of neurotransmitters such as serotonin and norepinephrine at nerve terminals [24].

Long-Term Treatment Concerns & Overprescription
Treatment with antidepressants can be short-term, long-term, or both. The short-term is characterized by the acute and continuation phases, while the long-term is characterized by the maintenance phase [26]. Depression is known to occur recurrently and is often managed in **primary care**, though the results vary in desirability. A review of studies from primary care depression cases found that patients undergoing long-term **pharmacological treatment** had varying, poor experiences with multiple relapses. On the other side, naturalistic studies found that patients who received **non-drug treatment** experienced no decline, and in some cases, experienced significant improvement. An article in the *American Psychological Association* described the issue of patients receiving drug treatments from their primary care providers, without consulting a mental health professional who may direct them to non-drug related treatments better suited to each individual [29].
Antidepressants are known to have **several side effects** ranging from sexual dysfunction, weight gain, and sleep difficulties to increased risk of osteoporosis, bleeding disorders, and diabetes (Ferguson, 2001). Antidepressant usage has even been linked to increased risk of **Parkinson's Disease (PD)**. A study in the UK found that an increased risk of PD was associated with patients who had undergone antidepressant treatment for at least ~2 years [25, 27].

Solutions

There is no simple solution to this problem with conflicting interests. After all, healthcare is unfortunately a business. Save for the case with Statins, the commonality between the other drugs' overprescription ties back to excess workload in primary care. These physicians are, on average, seeing ~20 patients daily amongst many other nonclinical duties such as paperwork [30]. Understandably, one can sympathize with a physician who may turn to prescribing a working medication as a quick means to an end so that they may get to each of their patients. However, even if the goal is to be able to provide care for each patient, quality is more important than quantity. Sadly, the physician workload problem is another problem of its own. Therefore, I propose an experimental solution that is very cost effective. Physicians should turn to the **Tenets of Osteopathic Medicine**, specifically: "the body is a unit; the person is a unit of body, mind, and spirit." Medical practice should emphasize the ability of the body to heal itself. Priority must be placed on non-drug treatment first, though this is easier for some pathologies than others (Some industries will certainly be unhappy with this). Consider the patient's lifestyle first and what changes can be made there before jumping to drug therapy. Also, try to educate patients on all the possible benefits and side effects (short-term and long-term, cite studies such as those included in this presentation) to drug treatments - this will allow for a shift in the current attitude towards healthcare (that there is a medicine for most conditions and patients can rely on these drugs without changing their lifestyle). Allow the patient to choose if the long-term side effects are worth the risk or if they would rather change their lifestyle and solve the problem naturally, and for good.

Literature Cited