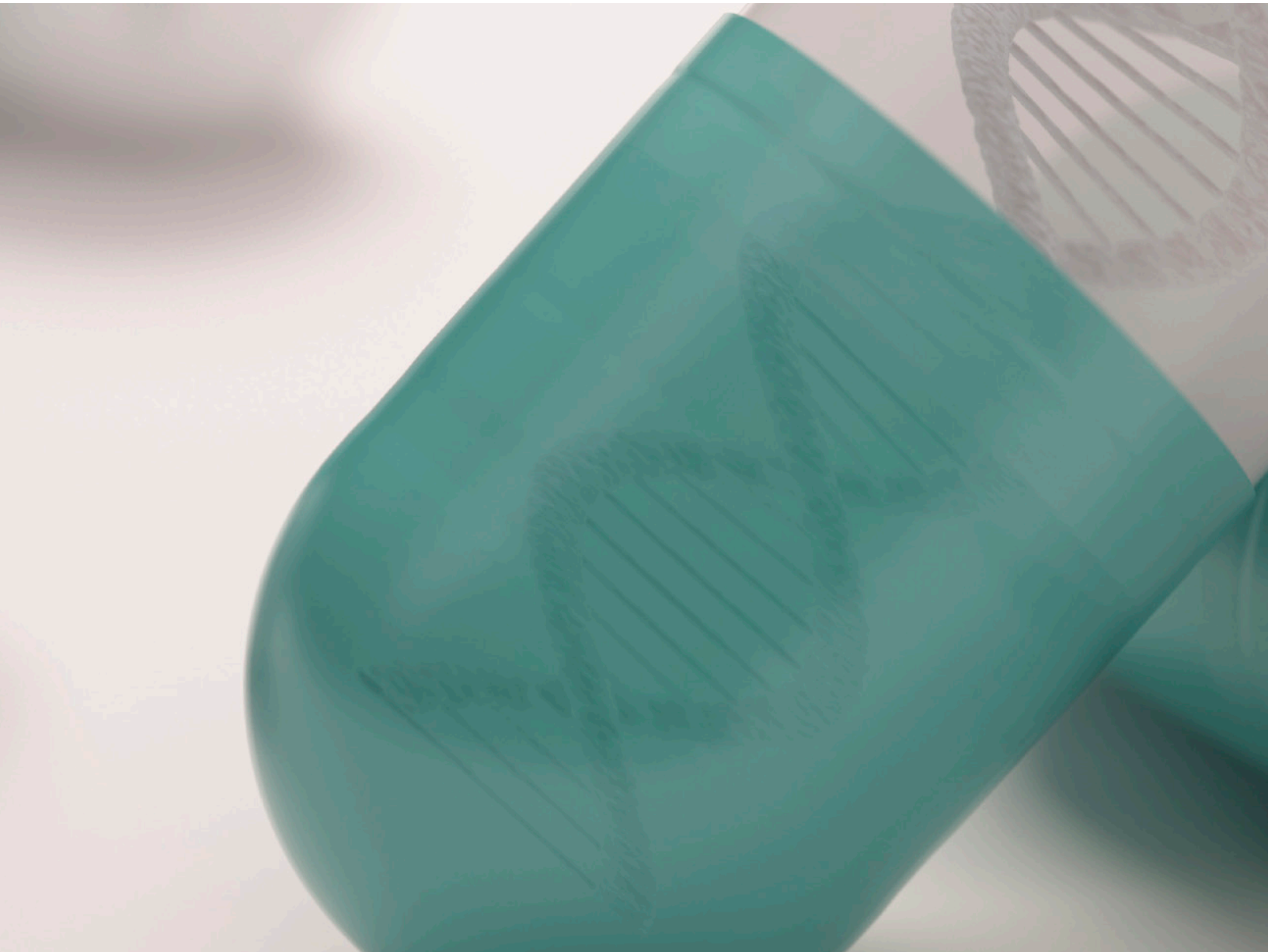
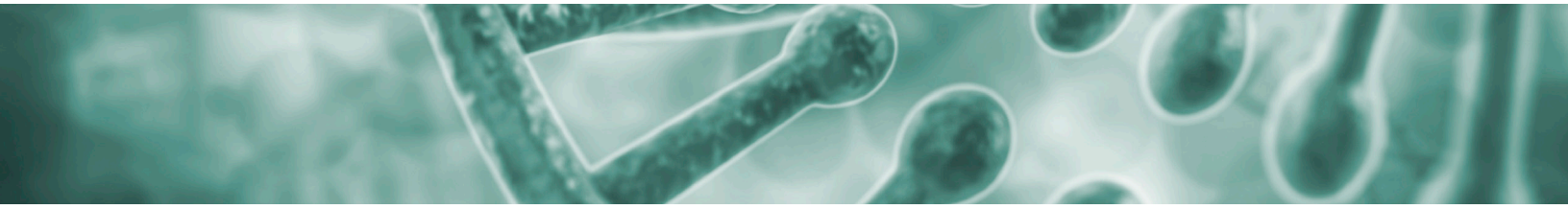
Clinical Reference Guide

GenTOX™



The War Against Polypharmacy: A New Cost-Effective Geriatric-Palliative Approach for Improving Drug Therapy in Disabled Elderly People - D. Garfinkel et al.



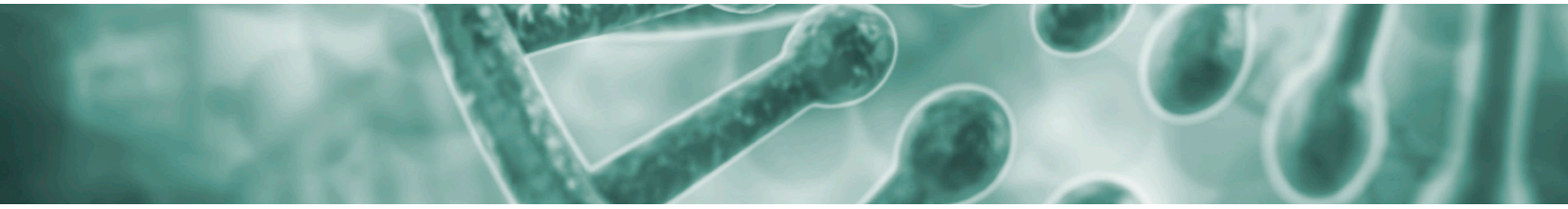
"Application of the geriatric-palliative methodology in the disabled elderly enables simultaneous discontinuation of several medications and yields a number of benefits: reduction in mortality rates and referrals to acute care facilities, lower costs, and improved quality of living."[1]

"A well-accepted indication in adults may be unclear, no longer in existence, or irrelevant in the elderly, particularly in nursing facilities. For example, a patient who has received an antihypertensive or nitrates when still independent and active may not need these drugs years later when already disabled and exerting minimal physical effort."[1]

"The rate of drug interactions is age related, the odds of inappropriate medication use are higher as the absolute number of medications prescribed increases, and the risk of hospitalization secondary to inappropriate medication use is much greater in these facilities than in the general population."[2,3,4,5]

"In the USA, for **every dollar** spent on medications used in nursing homes, **$1.33** is spent to manage drug-related problems."[6]

Using a Pharmacogenomic Algorithm to Guide the Treatment of Depression - D.K. Hall-Flavin et al.



"On average, there was a **7.2% reduction** in the QIDS-C16 score for study subjects in the unguided treatment group compared with a **31.2% reduction in overall score** for subjects in the guided group (P=0.002). Similarly, there was an **18.2% reduction** in HAM-D17 ratings for study subjects in the unguided group compared with a **30.8% reduction** for subjects in the guided group."[7]

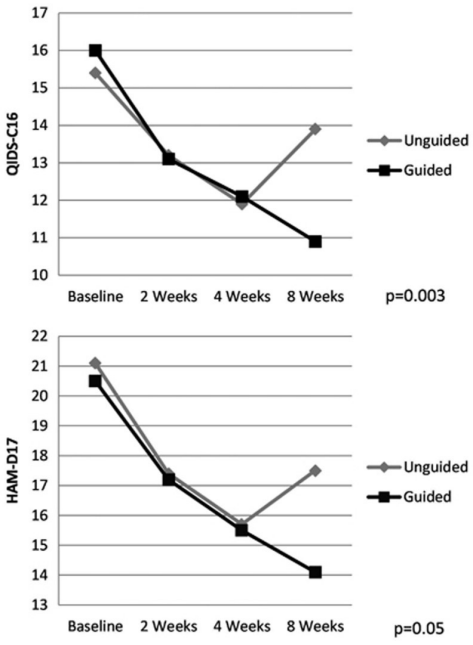
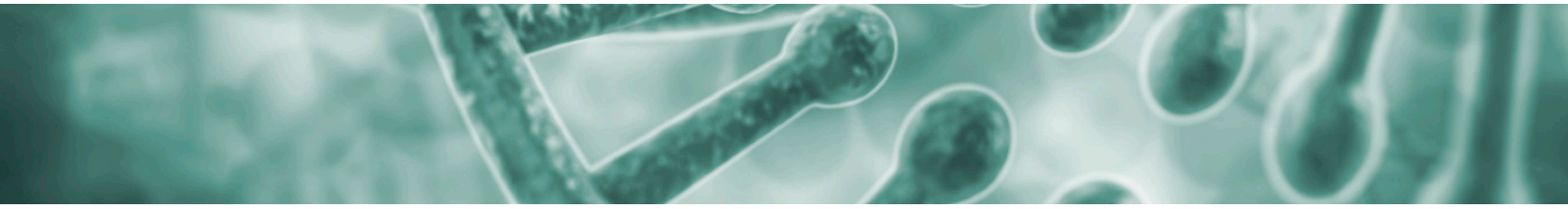


Figure 1 Depression scores using the Quick Inventory of Depressive Symptomalogy, Clinician Rated (QIDS-C16) and the 17-item Hamilton Rating Scale for Depression (HAM-D17) over the duration of the 8-week trial.

"A greater reduction in overall QIDS-C16 and HAM-D17 scores were achieved with pharmacogenomically guided treatment."[7]

A Naturalistic Study of the Effectiveness of Pharmacogenetic Testing to Guide Treatment in Psychiatric Patients with Mood and Anxiety Disorders - F. Brennan et al.



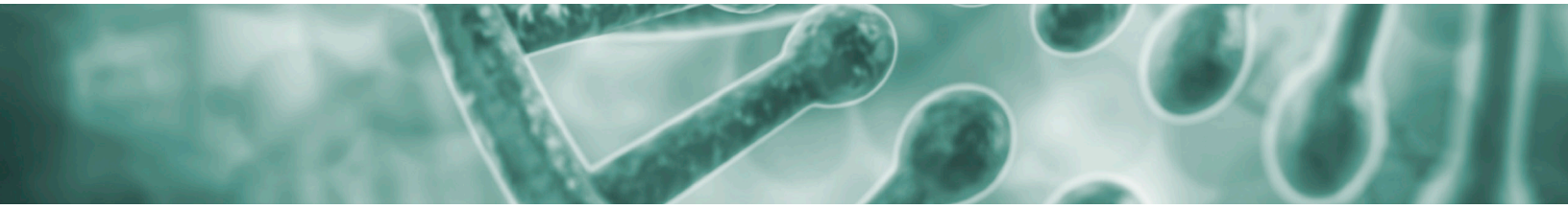
"These results suggest that a substantial proportion of individuals receiving pharmacogenetic testing showed clinically significant improvements on multiple measures of symptoms, adverse effects, and quality of life over 3 months. In the absence of a treatment-as-usual comparator, the proportion of improvement attributable to the test cannot be estimated."[8]

"A trial-and-error approach to prescribing has traditionally been utilized in psychiatry,12 contributing to the high costs of treatment and poor outcomes.13 Insight into a patient's genetic background may help clinicians identify appropriate treatment options by predicting the likelihood of drug response or adverse events."[8]

"Only 50% of patients with depression or anxiety will respond to first-line therapies."[8]

"Approximately **30% of US adults have a mental illness**,1 and almost half will develop one within their lifetime."[8]

Differences in Medicare Quality Measures Among Nursing Homes After Pharmacogenomic Testing - Newman RL, et al.



Medicare nursing home quality measure	Mean Pre-PGxT, all	Control NH, means			PGxT NH, means			Unadjusted Difference (PGxT- ontrols) ‡		Adjusted Difference (PGxT- ontrols) ‡	
		Pre-PGxT	Post-PGxT	Diff. (%) †	Pre-PGxT	Post-PGxT	Diff. (%)†	Est. (%)	p	Est. (%)	p
% of residents who self-report moderate to severe pain	5.3	5.2	4.9	-0.3 (-6%)	12.5	4.4	-8.0 (-151%)	-7.7 (-144%)	0.2	-5.4 (-101%)	0.001 *

PGxT= pharmacogenetic testing; "PGxT NH" = nursing homes that used pharmacogenetic testing with Pre-PGxT, being the period before actual pharmacogenetic testing and Post-PGxT, the period after testing. "Control NH" = control nursing homes that did not have pharmacogenetic testing, with Pre-PGxT and post PGxT being the matching time periods for the PGxT-NH that underwent actual pharmacogenetic testing.
†diff = difference, after PGxT testing minus before PGxT testing; ‡ difference of differences (PGxT difference minus control difference). (%) = the percentage values in the parentheses are the difference expressed in relative terms as % of the mean before testing (all nursing homes). Est. = estimated difference. The adjusted difference wasthe difference adjusted for region and baseline value. The two-sample t-test was used for the unadjusted analysis and linear regression was used for the adjusted analysis.

* $p < 0.05$.

Table 1 Changes in Medicare nursing home quality measures before and after PGxT in PGxT nursing homes versus control.

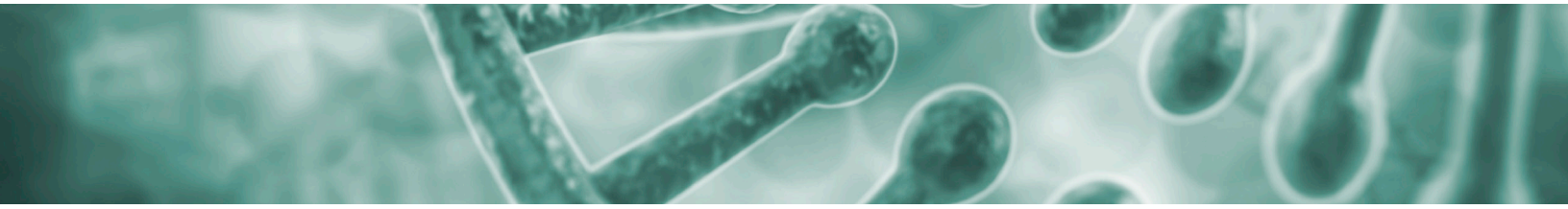
"There was a 5.4% reduction in self-reported, moderate-to-severe pain in the residents of the PGxT nursing home compared to control homes that did not initiate testing YouScript®, PGxT testing (p=0.001). There was also a tendency towards a reduction in falls resulting in major injury in the YouScript®, PGxT nursing homes when compared against the national average."[9]

"Specifically, in NY state, the mean±SE percentage of those who self-reported moderate to severe pain decreased substantially from 11.3 ± 6.3% to 3.1 ± 0.9% (-8.3 ± 6.2% change) among the three PGxT homes while it decreased only slightly from 3.5 ± 0.3% to 3.2 ± 0.3% (-0.2 ± 0.2% change) among the 159 control homes."[9]

"The prevalence of pain in nursing home residents is reported to be as high as 84%. Many reasons exist for the high prevalence of pain in the elderly, including degenerative musculoskeletal diseases, inflammation and arthritic pain, peripheral neuropathies, and side effects secondary to medications."[10-16]

"Residents referred for testing had been prescribed an average of 14.3 medications."[9]

Differences in Medicare Quality Measures Among Nursing Homes After Pharmacogenomic Testing - Newman RL, et al.



"Some common sequelae of pain include depression, anxiety, impaired mobility, falls, abdominal discomfort, reduced appetite, constipation, poor sleep, dys regulation of the immune-stress response, and delayed healing."[13]

"In our study, a number of drugs associated with a drug-drug, druggene or drug-drug-gene interaction were identified in the nursing homes that could have resulted in significant ADEs in the elderly".[9]

"Over-medication for pain with opioids or centrally acting drugs can result in falls and fall-related injuries, often requiring emergency room visits or hospitalizations. The three most commonly prescribed pain medications in the PGxT nursing homes were acetaminophen, oxycodone, and tramadol. When all the prescribed drugs were evaluated, the highest number of interaction warnings were observed with metoprolol, quetiapine, and simvastatin for all interactions and with metoprolol, warfarin, and clopidogrel for pharmacogenetic interactions."[15]

"In a recent study of older adults in the United States, the prevalence of recurrent falls in the past year (≥2 falls) was **19.5%** in participants with pain and **7.4%** in those without pain."[17]

Differences in Medicare Quality Measures Among Nursing Homes After Pharmacogenomic Testing - Newman RL, et al.

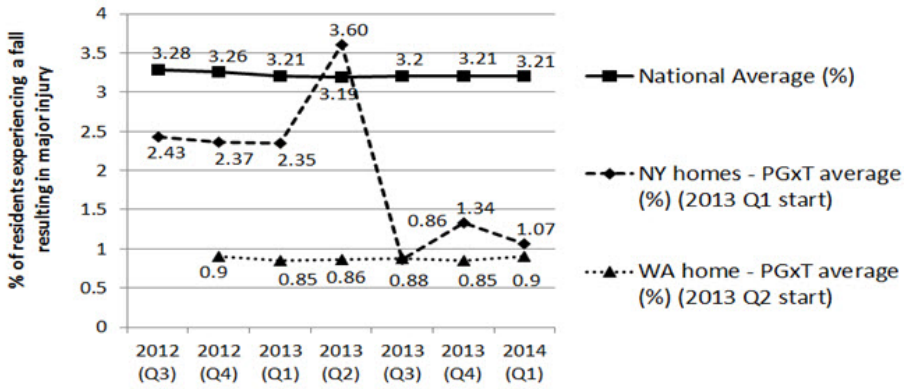


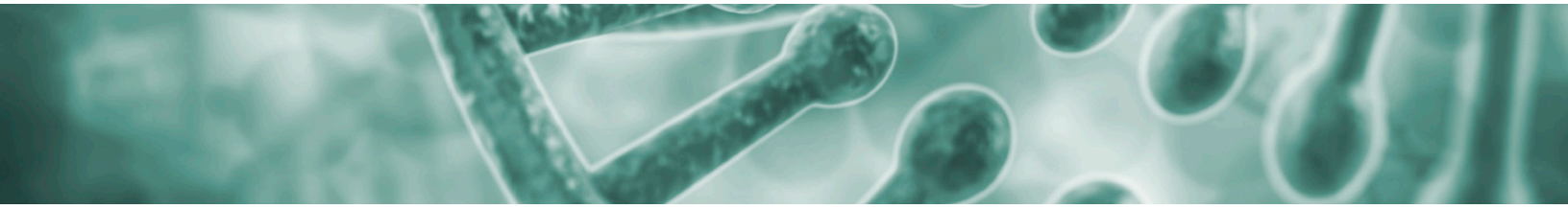
Figure 2 Percentage of residents experiencing a fall resulting in major injuries in PGxT homes compared to the average percentage of falls resulting in major injuries nationally in nursing homes. Note that there was a sharp reduction in falls-related major injuries in the nursing homes in New York (NY) after institution of PGxT.

"For the three New York homes that initiated PGxT, the average percentage of falls resulting in major injury was 2.43% six months pre-PGxT and 0.86% six months post-PGxT (64.52% relative risk reduction, 1.57% absolute risk reduction) compared to the national average of 3.28% in the same comparison, a larger reduction was shown in all four homes after PGxT compared to the national average trend."[18]

"A recent observational study of 205 elderly subjects that had undergone pharmacogentic testing demonstrated a 39% reduction in hospitalization and a 71% reduction in emergency department visits versus propensity score matched subjects from a registry who had not been tested."[19-20]

"Although this may seem insignificant, falls are a major cause of morbidity in the elderly and on average the hospitalization cost for a fall-related injury is **$34,294** (in 2012 dollars)."[18]

Cost-Effectiveness of One-Time Genetic Testing to Minimize Lifetime Adverse Drug Reactions - Reese ES, et al.



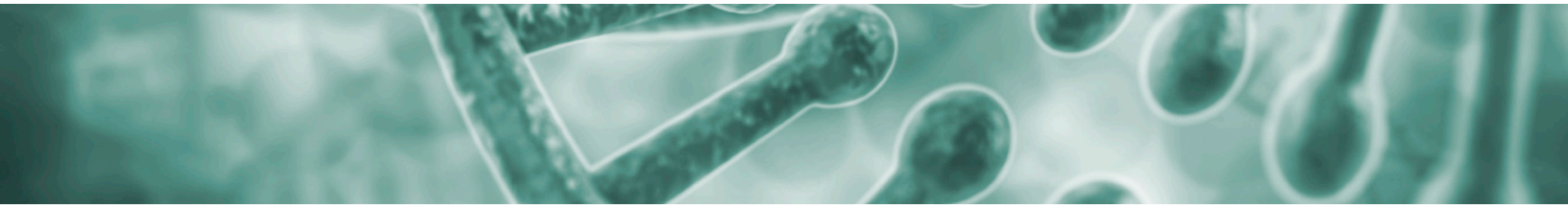
"There are three main types of economic evaluations in healthcare: cost-effectiveness, cost-utility and cost-benefit analyses."[21]

"One-time genetic testing had an incremental cost-effectiveness ratio (ICER) of $43,65."[21]

"Our Markov analysis implies that if we genetically test a group of 40-year olds and follow them until death, the ICER of genetic testing verses no testing would be $53 680 per additional QALY."

"The study by Bond and Raehl reported that the annual cost of adverse drug events for the Centers for Medicaid and Medicare Services (CMS) is ~$516 million."[21]

The Effect of Pharmacogenetic Profiling with a Clinical Decision Support Tool on Healthcare Resource Utilization and Estimated Costs in the Elderly Exposed to Polypharmacy - Brixner ES, et al.



"The model suggests that the cost of the test is nearly or completely offset by saving resulting from decreased healthcare resource utilization, providing evidence for the robustness of the model."[22]

"The saving increased to $2775 per year."[22]

"When the mean national data were used, the hypothetical model predicts a **$1132 saving.**"[22]

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