California Health Benefits Review Program

Analysis of California Assembly Bill 907 Coverage for PANDAS and PANS

A Report to the 2023–2024 California State Legislature

April 20, 2023
Key Findings
Analysis of California Assembly Bill 907
Coverage for PANDAS and PANS
Summary to the 2023–2024 California State Legislature, April 20, 2023

AT A GLANCE
The version of California Assembly Bill 907 analyzed by CHBRP would require health plans regulated by the Department of Managed Health Care (DMHC) and health policies regulated by the California Department of Insurance (CDI) to provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS).

In 2024, 100% of the 22.8 million Californians enrolled in state-regulated health insurance would have insurance subject to AB 907.

Benefit Coverage: At baseline, 100% of enrollees with health insurance subject to AB 907 have coverage that includes diagnostic tests recommended by various guidelines related to PANDAS/PANS and would continue to have 100% coverage postmandate. At baseline, 100% of enrollees with health insurance subject to AB 907 would have coverage for antibiotics, oral prescription immunomodulatory medications, and behavioral therapies and medications for managing neuropsychiatric symptoms, consistent with recommendations for treatment of PANDAS/PANS under existing clinical guidelines, and 0% have coverage for intravenous immunomodulating therapies, including plasma exchange and intravenous immunoglobulin (IVIG) therapy; postmandate 100% would have coverage for the aforementioned treatments. AB 907 would not be likely to exceed essential health benefits (EHBs).

Medical Effectiveness: CHBRP found insufficient evidence that the treatments recommended by clinical guidelines were effective at reducing or eliminating prominent symptoms of pediatric patients with PANDAS/PANS, with the exception of antibiotics and IVIG; the evidence of the effectiveness of these two treatments for eliminating or reducing symptoms was inconclusive.

Cost and Health Impacts: In 2024, AB 907 would result in approximately an additional $2.99 million (or 0.002%) in annual expenditures due to an estimated additional 90 enrollees utilizing IVIG, 0 additional enrollees utilizing plasma exchange, and an additional 22 enrollees utilizing other intravenous immunomodulating therapy (i.e., rituximab), as treatment for PANDAS/PANS. The public health impact of AB 907 is unknown due to insufficient and inconclusive evidence regarding the effectiveness of treatments for PANDAS/PANS.

CONTEXT
PANDAS/PANS are terms used to describe a subset of children with symptoms that include a sudden onset of obsessive-compulsive disorder (OCD) and/or tic disorders co-occurring with a collection of neuropsychiatric symptoms usually following an infection. Children may also become moody or irritable, or experience anxiety attacks, separation anxiety, rage, fatigue, phobias, insomnia, joint or muscle pain, or eating disorders.

PANDAS, currently classified as a subset of PANS, is hypothesized by some to be triggered by an autoimmune response to Group A Streptococcal bacteria (which cause strep throat or soft tissue infections). PANS is hypothesized to be triggered by causes other than Group A Streptococcus infection. Much remains unknown about PANDAS and PANS, and controversy remains regarding whether PANDAS differs enough from OCD/tic disorder and other neuropsychiatric disorders to warrant a different diagnostic category.

PANDAS/PANS has been primarily described in children between the ages of 3 and 12 years; however, the exact prevalence and age distribution of PANDAS/PANS is unknown. People over the age of 17 may also present with symptoms similar to those of PANDAS and PANS or have an initial diagnosis of either syndrome at a pediatric age that continues into adulthood. Because OCD is a required symptom for the diagnosis of

1 Similar cost and health impacts could be expected for the following year, though possible changes in medical science and other aspects of health make stability of impacts less certain as time goes by.
2 Refer to CHBRP’s full report for citations and references.
PANDAS and PANS, it is thought their prevalence can be estimated as a subset of the prevalence of pediatric OCD. Epidemiological research estimates that 0.5% to 5% of children in the United States are affected by OCD. One study estimates that 5% of children with OCD may meet the criteria for PANS/PANDAS.

CHBRP identified 3 clinical practice guidelines that meet AB 907’s criteria for diagnosing and treating patients with PANDAS/PANS, on which it based this analysis.

There is no specific diagnostic test to confirm a diagnosis for PANDAS or PANS, and other conditions may present with similar symptoms, making it a difficult to reliably diagnose and study PANDAS/PANS. Clinicians use a differential diagnostic process that includes collecting a patient’s medical history, conducting a physical exam, and may include diagnostic tests to rule out other conditions with similar symptoms. Additional tests may include testing for Group A Streptococcus, or Mycoplasma pneumoniae – infections that may be associated with PANDAS or PANS.

Per existing clinical guidelines, treatment options for PANDAS/PANS depend on the physical and/or neuropsychiatric symptoms experienced by the patient. The guidelines include treatments with: antibiotics; nonsteroidal anti-inflammatory drugs (NSAIDs); corticosteroids; cognitive behavioral therapy (CBT); psychotropics; intravenous immunoglobulin (IVIG); other immune-modulators (rituximab, mycophenolate mofetil); therapeutic plasma exchange; and vitamin D.

**BILL SUMMARY**

AB 907, as amended on March 16, 2023, would require Department of Managed Health Care (DMHC)-regulated health plans and California Department of Insurance (CDI)-regulated health policies to provide coverage for the prophylaxis, diagnosis, and treatment of PANDAS and PANS. Covered treatments must include antibiotics, medications and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin therapy. The bill also requires coverage to abide by several terms and conditions, including: 1) a prohibition on limitations to coverage for immunomodulating therapies for PANDAS/PANS in a manner inconsistent with clinical practice guidelines and evidence-based standards for diagnosis and treatment of PANDAS/PANS; and 2) a prohibition on a mandate for step therapy to treat only neuropsychiatric symptoms prior to authorization of coverage for immunomodulating therapies.

Figure A notes how many Californians have health insurance that would be subject to AB 907.

**Figure A. Health Insurance in CA and AB 907**


Key: CDI = California Department of Insurance; COHS = County Organized Health System; DMHC = Department of Managed Health Care.

**IMPACTS**

**Medical Effectiveness**

CHBRP analyzed the strength of evidence for the effectiveness of antibiotics, psychotropic medications, cognitive behavioral therapy, plasma exchange, IVIG and other immunomodulating medications addressed by AB 907, specifically, for children affected by PANDAS/PANS.

Overall, the evidence is insufficient or inconclusive that any of these treatments are effective at reducing prominent symptoms, such as OCD symptoms, tics, or eating restrictions, for pediatric patients with PANDAS/PANS.

The body of research on PANDAS and PANS is small (number of studies and sample sizes of available studies) compared with many other diseases and conditions. Additional studies involving controlled clinical trials, larger sample sizes, and clear eligibility criteria are necessary to determine which treatments are effective for children with PANDAS/PANS.
More specifically, CHBRP found insufficient evidence on the effectiveness of CBT, psychotropics, NSAIDs, corticosteroids, plasma exchange, rituximab, mycophenolate mofetil, and vitamin D in reducing or eliminating the prominent symptoms associated with PANDAS/PANS.

CHBRP found inconclusive evidence on the effectiveness of antibiotics and IVIG in reducing or eliminating the prominent symptoms associated with PANDAS/PANS.

Each of the medications reviewed for this analysis is associated with a variety of side effects and harms. See Table 3 of the full report for more details.

**Benefit Coverage, Utilization, and Cost**

**Benefit Coverage**

At baseline, 100% of enrollees with health insurance that would be subject to AB 907 have coverage that includes diagnostic tests associated with PANDAS/PANS recommended by various guidelines for diagnosing PANDAS/PANS.

At baseline, 100% of enrollees with health insurance that would be subject to AB 907 have coverage that includes some, but not all, treatments for PANDAS/PANS. Coverage by type of treatment varies substantially.

CHBRP found that 100% of enrollees have health insurance that includes antibiotics commonly used for PANDAS/PANS and some oral prescription immunomodulatory medications including steroids and nonsteroidal anti-inflammatory medications (NSAIDs).

Similarly, 100% of enrollees have health insurance that includes coverage for psychotropics used for treatment of neuropsychiatric symptoms of PANDAS/PANS, including selective serotonin receptor inhibitors (SSRIs), benzodiazepines, and antipsychotics. One hundred percent of enrollees also have health insurance that includes coverage of behavioral health therapies used for treatment of neuropsychiatric symptoms of PANDAS/PANS, including cognitive behavioral therapy (CBT). CHBRP finds that 0% of enrollees have coverage for intravenous immunomodulating therapies, including plasma exchange, B-cell modulators (rituximab), and intravenous immunoglobulin (IVIG) therapy.

Postmandate, 100% of enrollees with health insurance subject to AB 907 would have coverage for all diagnostic tests and treatments included under the bill.

**Utilization**

CHBRP estimates that at baseline, 15,410 enrollees use diagnostic tests for PANDAS/PANS. These include various blood tests, throat cultures, and nose swabs. CHBRP estimates that for every 23 children tested for PANDAS/PANS using these diagnostic tests, 1 child is diagnosed with PANDAS/PANS and 22 children are not given this diagnosis. Given that 100% of enrollees already have baseline coverage, CHBRP estimates no changes in utilization for these diagnostic tests.

At baseline, CHBRP estimates that 670 enrollees have a PANDAS/PANS diagnosis. Among these enrollees, average annual utilization of oral prescription medications used for the treatment and management of neuropsychiatric symptoms (including medications such as antibiotics, steroids, NSAIDs, and psychotropics) is 17.8 prescriptions, each with a 30-day supply. At baseline, annual utilization of CBT is 20 visits per year. Given that 100% of enrollees already have baseline coverage for these medications and behavioral health therapies such as CBT, CHBRP estimated no changes in utilization of these specific medications and CBT services postmandate.

CHBRP estimates that IVIG, rituximab, and plasma exchange have extremely limited use at baseline. CHBRP estimates that average annual utilization of IVIG among all enrollees with PANDAS/PANS would increase to 0.7 infusion therapy sessions per year. This results in an estimated 90 enrollees with moderate or severe PANDAS/PANS utilizing IVIG at least once per year, with greater expected utilization among those with severe PANDAS/PANS. CHBRP estimates that average annual utilization of rituximab would increase to 0.1 infusion therapy sessions. This results in an estimated 22 enrollees with severe PANDAS/PANS utilizing an estimated average of 3 rituximab infusions per year. CHBRP estimated no change in the use of plasma exchange services given their low availability and the lack of evidence of their effectiveness in PANDAS/PANS.

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3 *Insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

4 *Inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.
Key Findings: Analysis of California Assembly Bill 907

Expenditures

AB 907 would increase total net annual expenditures by total net annual $2,990,000 or total net annual 0.0020% for enrollees with DMHC-regulated plans (including DMHC-regulated Medi-Cal) and CDI-regulated policies.

Figure B. Expenditure Impacts of AB 907


Medi-Cal

For this analysis, CHBRP has included potential impacts on Medi-Cal beneficiaries. In addition to the expected increase of $1.47 million in premiums CHBRP is estimating for the 8.8 million Medi-Cal beneficiaries enrolled in DMHC-regulated plans (a figure that represents a 0.005% increase in premiums), it seems reasonable to assume that a population proportional increase of $370,000 would occur for the 2.0 million beneficiaries enrolled in county organized health systems (COHS) managed care.

CalPERS

For enrollees associated with CalPERS in DMHC-regulated plans, premiums would increase by 0.001% ($0.01 per member per month, or $83,000 total increase in expenditures).

Covered California – Individually Purchased

Premiums for enrollees in individual plans purchased through Covered California would increase by a total of $69,000 in annual expenditures.

Number of Uninsured in California

Because the change in average premiums does not exceed 1% for any market segment, CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of AB 907.

Public Health

In the first year postmandate, the public health impact of AB 907 is unknown due to insufficient and inconclusive evidence regarding the effectiveness of treatments for PANDAS/PANS. Please note that the absence of evidence is not “evidence of no effect.” It is possible that an impact – desirable or undesirable – could result, but current evidence is insufficient to inform an estimate.

Long-Term Impacts

Utilization of diagnostic tests and treatments for PANDAS/PANS is expected to be similar in the long term as utilization in the first 12 months postmandate. However, should evidence about the effectiveness of new diagnostic tests or treatments such as IVIG or rituximab become more conclusive, for example, via more evidence from larger randomized controlled clinical trials, more physicians may prescribe these treatments.

Cost impacts are expected to also be similar to those projected in the first 12 months postmandate.

Due to the dearth of research about PANDAS/PANS, CHBRP finds an unknown public health impact of AB 907 over the long term.

Essential Health Benefits and the Affordable Care Act

AB 907 would not require coverage for a new state benefit mandate that appears to exceed the definition of EHBS in California.
A Report to the California State Legislature

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April 20, 2023

California Health Benefits Review Program
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The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

An analytic staff based at the University of California, Berkeley, supports a task force of faculty and research staff from multiple University of California campuses to complete each CHBRP analysis. A strict conflict-of-interest policy ensures that the analyses are undertaken without bias. A certified, independent actuary helps to estimate the financial impact. Content experts with comprehensive subject-matter expertise are consulted to provide essential background and input on the analytic approach for each report.

More detailed information on CHBRP’s analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.
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### Table 1. Impacts of AB 907 on Benefit Coverage, Utilization, and Cost, 2024

<table>
<thead>
<tr>
<th>Benefit coverage</th>
<th>Baseline (2024)</th>
<th>Postmandate Year 1 (2024)</th>
<th>Increase/Decrease</th>
<th>Change Postmandate</th>
</tr>
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<tbody>
<tr>
<td>Total enrollees with health insurance subject to state-level benefit mandates (a)</td>
<td>22,842,000</td>
<td>22,842,000</td>
<td>—</td>
<td>0.00%</td>
</tr>
<tr>
<td>Total enrollees with health insurance subject to AB 907</td>
<td>22,842,000</td>
<td>22,842,000</td>
<td>—</td>
<td>0.00%</td>
</tr>
<tr>
<td>Total percentage of enrollees with coverage for diagnostics/treatment of PANDAS/PANS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnostics (b)</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Oral prescription medications (30-day supply) (c) (d)</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Psychology visits (CBT)</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Immunomodulating infusion therapy – rituximab</td>
<td>0%</td>
<td>100%</td>
<td>100%</td>
<td>N/A</td>
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<tr>
<td>Immunomodulating infusion therapy – IVIG session</td>
<td>0%</td>
<td>100%</td>
<td>100%</td>
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<td>Plasma exchange</td>
<td>0%</td>
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<td>100%</td>
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<td>Utilization and cost</td>
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<td>Number of enrollees diagnosed with PANDAS/PANS</td>
<td>670</td>
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<td>—</td>
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<td>Diagnostics (b)</td>
<td>210.0</td>
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<td>—</td>
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<td>Oral prescription medications (30-day supply) (c) (d)</td>
<td>17.8</td>
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<td>Psychology visits (CBT)</td>
<td>20.0</td>
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<tr>
<td>Immunomodulating infusion therapy – rituximab (e)</td>
<td>0.1</td>
<td>0.1</td>
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<td>Immunomodulating infusion therapy – IVIG session (e)</td>
<td>0.7</td>
<td>0.7</td>
<td>0.00%</td>
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<tr>
<td>Plasma exchange session (f)</td>
<td>0.7</td>
<td>0.7</td>
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<td>Average unit cost of the following PANDAS/PANS-related services:</td>
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<td>Diagnostics (b)</td>
<td>$30</td>
<td>$30</td>
<td>—</td>
<td>0.00%</td>
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<td>Oral prescription medications (30-day supply) (c) (d)</td>
<td>$7</td>
<td>$7</td>
<td>—</td>
<td>0.00%</td>
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<td>Psychology visits (CBT)</td>
<td>$142</td>
<td>$142</td>
<td>—</td>
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<td>Immunomodulating infusion therapy – rituximab</td>
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<td>$9,566</td>
<td>—</td>
<td>0.00%</td>
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<td>Immunomodulating infusion therapy – IVIG session</td>
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<td>Plasma exchange session</td>
<td>$2,136</td>
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<td>—</td>
<td>0.00%</td>
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<td>Expenditures</td>
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<td>Premiums</td>
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<td>Employer-sponsored (g)</td>
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<td>$57,648,888,000</td>
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<td>CalPERS employer (h)</td>
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<td>$6,158,345,000</td>
<td>$83,000</td>
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<td>Medi-Cal (excludes COHS) (i)</td>
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<td>$29,619,854,000</td>
<td>$1,471,000</td>
<td>0.005%</td>
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*Expendees premiums (expenditures)*
Enrollees, individually purchased insurance

<table>
<thead>
<tr>
<th></th>
<th>Current</th>
<th>Prior Year</th>
<th>Percent Change</th>
<th>PMPM Percent Change</th>
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<tr>
<td>Outside Covered California</td>
<td>$21,229,233,000</td>
<td>$21,229,347,000</td>
<td>$114,000</td>
<td>0.001%</td>
</tr>
<tr>
<td>Through Covered California</td>
<td>$16,361,278,000</td>
<td>$16,361,347,000</td>
<td>$69,000</td>
<td>0.000%</td>
</tr>
<tr>
<td>Enrollees, group insurance (j)</td>
<td>$18,263,775,000</td>
<td>$18,264,049,000</td>
<td>$274,000</td>
<td>0.002%</td>
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</table>

Enrollee out-of-pocket expenses

<table>
<thead>
<tr>
<th>Cost sharing for covered benefits (deductibles, copayments, etc.)</th>
<th>Current</th>
<th>Prior Year</th>
<th>Percent Change</th>
<th>PMPM Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>$21,229,233,000</td>
<td>$21,229,347,000</td>
<td>$114,000</td>
<td>0.001%</td>
<td></td>
</tr>
</tbody>
</table>

Outside Covered California $4,867,955,000 $4,868,000,000 $45,000 0.001%

Through Covered California $16,361,278,000 $16,361,347,000 $69,000 0.000%

Enrollees, group insurance (j) $18,263,775,000 $18,264,049,000 $274,000 0.002%

Expenses for noncovered benefits (k) (l)

<table>
<thead>
<tr>
<th>Costs</th>
<th>Current</th>
<th>Prior Year</th>
<th>Percent Change</th>
<th>PMPM Percent Change</th>
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<td>$13,857,141,000</td>
<td>$13,857,294,000</td>
<td>$153,000</td>
<td>0.001%</td>
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</table>

$0 $0 $0 0.00%

Total expenditures $146,774,787,000 $146,777,777,000 $2,990,000 0.002%


Notes:
(a) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California, CalPERS, or Medi-Cal. 5
(b) Diagnostics include various blood tests, throat cultures, and nose swabs. See Appendix C for more details. CHBRP estimates that 15,410 enrollees ages 0-17 have diagnostic tests used as for PANDAS/PANS diagnosis each year. Of every 23 enrollees who undergo diagnostic tests, CHBRP estimates that 1 enrollee is diagnosed with PANDAS/PANS, and 22 enrollees are not given this diagnosis.
(c) Although mycophenolate mofetil is included in the PANDAS/PANS guidelines, we excluded it from our analysis based on discussions with physicians in the field.
(d) Oral prescription medications include antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs, selective serotonin uptake inhibitors, benzodiazepines, and antipsychotics. See Appendix C for more details.
(e) The percent changes postmandate for rituximab and IVIG are greater than zero, but appear to be zero in the table due to rounding.
(f) Utilization for plasma exchange session is not projected to change due to a variety of supply issues, as discussed in the report.
(g) In some cases, a union or other organization. Excludes CalPERS.
(h) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.1% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC. 6 CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).
(i) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. In addition, CHBRP is estimating that there would also be a proportional increase of $0.37 million for Medi-Cal beneficiaries enrolled in COHS managed care.
(j) Enrollee premium expenditures include contributions by enrollees to employer (or union or other organization)-sponsored health insurance, health insurance purchased through Covered California, and any contributions to enrollment through Medi-Cal to a DMHC-regulated plan.
(k) Includes only expenses paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered postmandate. Other components of expenditures in this table include all health care services covered by insurance.
(l) For covered benefits, such expenses would be eliminated, although enrollees with newly compliant benefit coverage might pay some expenses if benefit coverage is denied (through utilization management review).

Key: CalPERS = California Public Employees' Retirement System; CBT = cognitive behavioral therapy; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care; IVIG = intravenous immunoglobulin; PANDAS = Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections; PANS = Pediatric Acute-onset Neuropsychiatric Syndrome.

5 For more detail, see CHBRP’s resource, Sources of Health Insurance in California, available at http://chbrp.org/other_publications/index.php.
POLICY CONTEXT

The California Assembly Committee on Health has requested that the California Health Benefits Review Program (CHBRP) conduct an evidence-based assessment of the medical, financial, and public health impacts of AB 907, coverage of PANDAS and PANS, as amended on March 16, 2023.

Bill-Specific Analysis of AB 907, Coverage of PANDAS and PANS

Bill Language

AB 907, as amended on March 16, 2023, would require health plans regulated by the Department of Managed Health Care (DMHC) and health policies regulated by the California Department of Insurance (CDI) to provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). Covered treatments must include antibiotics, medications and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin (IVIG) therapy.

The bill also requires coverage to abide by the following terms and conditions:

- Prohibition on cost sharing being greater than that applied to other benefits provided by the contract or policy.
- Coverage would be required to be provided in a timely manner. Denials or delays in coverage for PANDAS or PANS therapies would be prohibited, if the denial or delay was because the enrollee was diagnosed with, or previously received treatment for, a condition under a different diagnostic name, including autoimmune encephalopathy.
- Prohibition on limitations to coverage for immunomodulating therapies for PANDAS/PANS in a manner inconsistent with clinical practice guidelines and evidence-based standards for diagnosis and treatment of PANDAS/PANS.
- Prohibition on a mandate for step therapy to treat only neuropsychiatric symptoms prior to authorization of coverage for immunomodulating therapies.
- Coverage would be required to adhere to treatment recommendations developed by a consortium of medical professionals convened to research, identify, and publish clinical practice guidelines and evidence-based standards for the diagnosis and treatment of PANDAS and PANS.

AB 907 also requires PANDAS and PANS to be coded as autoimmune encephalitis for the purposes of billing and diagnosis, until the American Medical Association and the federal Centers for Medicare and Medicaid Services (CMS) create and assign a specific code for PANDAS and PANS. Once created, the bill allows for PANDAS and PANS to be coded as either the specific codes or autoimmune encephalitis.

The full text of AB 907, as introduced, can be found in Appendix A.

Relevant Populations

If enacted, AB 907 would apply to the health insurance of approximately 22.8 million enrollees (58.6% of all Californians). This represents all Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law, which includes health insurance regulated

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by the DMHC or the CDI. If enacted, the law would apply to the health insurance of enrollees in DMHC-regulated plans and CDI-regulated policies, including DMHC-regulated Medi-Cal plans.

As of January 1, 2022, outpatient prescription drugs are covered on a fee-for-service basis by the California Department of Health Care Services (DHCS) for all Medi-Cal beneficiaries.\(^8\) Their pharmacy benefit is “carved out” of the coverage provided by Medi-Cal managed care plans, and so AB 907 would not be expected to impact their outpatient prescription drug benefit coverage.

**Analytic Approach and Key Assumptions**

CHBRP used the guidelines developed by the PANDAS Physicians Network (PPN), the PANDAS/PANS Clinical Research Consortium, and Nordic Pediatric Immunopsychiatry Group in its analytic approach to AB 907 (Chang et al., 2015; Cooperstock et al., 2017; Frankovich et al., 2017; Pfeiffer et al., 2021; Thienemann et al., 2017). More information is provided in the *Background on PANDAS and PANS* section. CHBRP’s analysis uses these guidelines to support its analytic approach but notes that revisions or future guidelines may differ from those used for this analysis. Table 2 shows the treatments required by AB 907 and those included in the guidelines mentioned above.

It should be noted that the language of AB 907 requires coverage of PANDAS and PANS to adhere to treatment recommendations in clinical practice guidelines and evidence-based standards; the guidelines developed by the aforementioned groups are consensus guidelines. Evidence-based guidelines make statements that are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative options. Consensus guidelines are developed by an independent panel of experts with experience in the condition(s), usually multidisciplinary, convened to review the research literature in an evidence-based manner for the purpose of advancing the understanding of an issue, procedure or method (Jacobs et al, 2014). The key difference between the development of the two types of guidelines appears to be that when the evidence is of high quality, some guideline panels rely on the evidence review to guide their recommendations and the process is evidence-based. However, when the evidence is very limited and hence of low quality or very low quality, some guideline panels rely primarily on clinical experience and the process is consensus-based (Yao et al, 2021).

Table 2 also shows whether the treatments under AB 907 would fall under the medical or pharmacy benefit. Drugs that are physician-ordered and administered under the supervision of a physician – generally in a hospital, a provider’s office, infusion center, or similar medical facility – along with the hospital stay or office visit are generally covered through a medical benefit. The intravenous immunomodulating therapies discussed in this analysis would fall into this category and are assumed to be covered under the medical benefit. Pharmacy benefits cover outpatient prescription drugs by covering prescriptions that are generally filled at a retail pharmacy, a mail-order pharmacy, or a specialty pharmacy.

**Table 2. Treatments Considered for AB 907 Analysis**

<table>
<thead>
<tr>
<th>Treatment Required by AB 907</th>
<th>Medications/Treatment From Clinical Guidelines</th>
<th>Benefit Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Azithromycin, penicillin</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>Behavioral therapies to manage neuropsychiatric symptoms</td>
<td>Cognitive behavioral therapy</td>
<td>Medical</td>
</tr>
</tbody>
</table>

CHBRP uses the age range of 0 to 17 years throughout this analysis because the diagnostic criteria for PANDAS and PANS include pediatric onset (Chang et al., 2013; NIMH, 2019). However, CHBRP recognizes that people over the age of 17 may also present symptoms similar to those of PANDAS and PANS or have an initial diagnosis of either syndrome at a pediatric age that continues into adulthood.

CHBRP assumed that if AB 907 was enacted, cost sharing for treatments outlined in the bill would not change and that DMHC-regulated plans and CDI-regulated policies would require prior authorization for some treatments.

The California Department of Health Care Services (DHCS) began implementation of the California Advancing and Innovating Medi-Cal (CalAIM) initiative in 2022. To the extent possible for this analysis, CHBRP has incorporated known CalAIM changes into its methods and approach.

### Interaction With Existing State and Federal Requirements

Health benefit mandates may interact and align with the following state and federal mandates or provisions.

#### California Policy Landscape

**California law and regulations**

The California Legislature has not previously introduced mandates related to PANDAS or PANS. In 2018, California passed a resolution proclaiming October 9 as PANS awareness day.

CHBRP reviewed the state’s Independent Medical Review (IMR) determinations since the implementation of the Affordable Care Act (ACA) in California and found 29 related to coverage of treatment for PANDAS, PANS, and autoimmune encephalitis. All determinations were specific to coverage of IVIG. A total of 15 IMRs overturned the decision of the health plan for enrollees requesting coverage for IVIG, based on the refractory nature of the patient’s condition and sufficient evidence showing lack of improvement following first-line therapies. The health plans’ decisions were upheld in 14 instances where enrollees requested coverage of IVIG either due to insufficient medical evidence and/or lack of clinical evidence supporting the patient’s diagnosis and therefore medical necessity\(^9\) for the treatment. CHBRP found 5 determinations specific to the diagnosis of PANDAS and PANS. None of the medical reviews were for coverage requests of diagnostic tests or services recommended by any of the guidelines used by CHBRP for this analysis.

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\(^9\) A medically necessary treatment or service is one that is appropriate and consistent with a patient's diagnosis and that, in accordance with locally accepted standards of practice, cannot be omitted without adversely affecting the patient's condition or quality of care.
Similar requirements in other states

There are 10 states, including Arkansas, Delaware, Illinois, Indiana, Kansas, Maryland, Massachusetts, Minnesota, New Hampshire, and Rhode Island, that mandate at least temporary coverage of treatment for PANDAS and PANS. Arkansas mandates health plans cover the off-label use of drug treatment to treat PANS and PANDAS, but allows for cost sharing and prior authorization requirements. Delaware, Illinois, Indiana, and Maryland mandate coverage but only specify that IVIG must be covered. Massachusetts also only specifies IVIG must be covered, and sets up an advisory council on PANDAS and PANS. Kansas, New Hampshire, and Rhode Island allow for temporary coverage of treatment for PANDAS and PANS until December 31, 2023; July 1, 2024; and December 31, 2025, respectively. Minnesota’s law is most similar to AB 907, describing the same set of treatments that may be recommended by a health care professional for PANDAS and PANS.

This year, 12 states in addition to California (Arkansas, Connecticut, Georgia, Illinois, Maine, Massachusetts, Missouri, New York, Oregon, Rhode Island, Texas, and West Virginia) have introduced legislation this year related to PANDAS and PANS. Arkansas’ and Illinois’ legislation would amend their existing laws to specify conditions under which IVIG and other treatment coverage must be provided. Rhode Island’s legislation would have extended the sunset for coverage for treatment but was held for further study. Massachusetts’ bill would order a study to be conducted related to PANDAS and PANS in conjunction with its PANS advisory council. Georgia’s legislation would establish a 3-year pilot program to provide coverage for the diagnosis and treatment of PANDAS and PANS, beginning in 2025. The Missouri and Oregon bills would specify coverage for IVIG treatments, and Maine’s bill would provide coverage for the similar treatments as those mandated in AB 907. New York and Connecticut’s legislation would mandate coverage for unspecified treatment of PANS. Texas’ bill would establish PANS advisory council. West Virginia’s legislation mandates coverage for IVIG for PANDAS and PANS and other autoimmune encephalopathies only if prior authorization is obtained by showing all other treatments have been exhausted.

Federal Policy Landscape

Affordable Care Act

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how AB 907 may interact with requirements of the ACA as presently

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10 The term off-label refers to use of a drug in a way that differs from the specifications explicitly approved by the Food and Drug Administration (FDA). Off-label use of drugs is not uncommon and is discussed by the FDA on a webpage intended for patients. See www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label. Accessed March 13, 2023. The FDA’s specifications may include particular drug dosages (a measurement, often in milligrams) or particular dosage forms (oral vs. inhaled, extended vs. immediate release, ocular vs. oral, etc.).
13 Massachusetts General Laws 176G §4GG, 175 §47NN, 176B §400, 32A §17R, 176A §800, 111 §242.
14 Minnesota Code §62A.3097.
15 Arkansas Senate Bill (SB) 181; Illinois SB 101.
16 Rhode Island SB 0024 and House Bill (HB) 5256.
17 Massachusetts SB 1266.
18 Georgia House Bill 140.
19 Oregon SB 628; Missouri HB 1365; Maine HB 663.
20 New York SB 3038 and Assembly Bill 2823; Connecticut SB 452.
21 Texas HB 3808 and SB 1185.
22 West Virginia SB 45.
exist in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).  

**Essential Health Benefits**

In California, nongrandfathered individual and small-group health insurance is generally required to cover essential health benefits (EHBs). In 2024, approximately 12.1% of all Californians will be enrolled in a plan or policy that must cover EHBs.

States may require state-regulated health insurance to offer benefits that exceed EHBs. Should California do so, the state could be required to defray the cost of additionally mandated benefits for enrollees in health plans or policies purchased through Covered California, the state’s health insurance marketplace. However, state benefit mandates specifying provider types, cost sharing, or other details of existing benefit coverage would not meet the definition of state benefit mandates that could exceed EHBs.

AB 907 would not require coverage for a new state benefit mandate that appears to exceed the definition of EHBs in California.

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23 The ACA requires nongrandfathered small-group and individual market health insurance — including, but not limited to, qualified health plans sold in Covered California — to cover 10 specified categories of EHBs. Policy and issue briefs on EHBs and other ACA impacts are available on the CHBRP website: [www.chbrp.org/other_publications/index.php](http://www.chbrp.org/other_publications/index.php).

24 Although many provisions of the ACA have been codified in California law, the ACA was established by the federal government, and therefore, CHBRP generally discusses the ACA as a federal law.

25 A grandfathered health plan is “a group health plan that was created – or an individual health insurance policy that was purchased – on or before March 23, 2010. Plans or policies may lose their ‘grandfathered’ status if they make certain significant changes that reduce benefits or increase costs to consumers.” Available at: [www.healthcare.gov/glossary/grandfathered-health-plan](http://www.healthcare.gov/glossary/grandfathered-health-plan).


28 ACA Section 1311(d)(3).


30 However, as laid out in the Final Rule on EHBs U.S. Department of Health and Human Services (HHS) released in February 2013, state benefit mandates enacted on or before December 31, 2011, would be included in the state’s EHBs, and there would be no requirement that the state defray the costs of those state-mandated benefits. For state benefit mandates enacted after December 31, 2011, that are identified as exceeding EHBs, the state would be required to defray the cost.


32 Both Massachusetts and Utah currently pay defrayment costs for exceeding EHBs (Maine Bureau of Insurance, 2023).
BACKGROUND ON PANDAS AND PANS

AB 907 would require Department of Managed Health Care (DMHC)-regulated health plans and California Department of Insurance (CDI)-regulated policies to provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). The treatments covered under this bill would include:

- Antibiotics;
- Medications and behavioral therapies to manage neuropsychiatric symptoms;
- Immunomodulating medicines;
- Plasma exchange; and
- Intravenous immunoglobulin therapy (IVIG).

This section explains the terms PANDAS and PANS, provides an overview of the diagnostic criteria and treatments based on available clinical practice guidelines, and describes the prevalence and incidence of the disease in California.

What Are PANS and PANDAS?

Identified in the published peer-reviewed literature in 1998, PANDAS/PANS are terms used to describe a subset of children with symptoms that include a sudden onset of a collection of neuropsychiatric symptoms co-occurring with obsessive-compulsive disorder (OCD) and/or tic disorders usually following an infection (NIMH, 2019; Pichichero et al., 2023; PPN, 2023c).

PANDAS, currently classified as a subset of PANS, is hypothesized by some to be triggered by an autoimmune response to Group A Streptococcal (Strep) bacteria (which cause strep throat or soft tissue infections). More specifically, some research hypothesizes that the body’s immune system may produce antibodies (known as cross-reactive antibodies) that create a dysfunctional autoimmune response following a Group A Strep infection, which may result in a range of conditions, including rheumatic fever which affects the heart valves. These cross-reactive antibodies may occur in the brain, where the autoimmune response is thought to result in sudden onset of neuropsychiatric symptoms such as OCD, tic disorders, and other psychiatric symptoms that also present in children diagnosed with PANDAS (NIMH, 2019). However, findings from other studies run counter to this hypothesis. Two prospective, blinded case-control studies have shown no observable temporal relationship between Group A Strep infection and the clinical exacerbations (i.e., worsening or increase in symptoms) associated with patients who met published diagnostic criteria for PANDAS (Kurlan et al., 2008; Leckman et al., 2011).

PANS is hypothesized to be triggered by causes other than Group A Streptococcus infection (Calaprice et al., 2017; NIMH, 2019; PPN, 2023c).

Much remains unknown about PANDAS and PANS and controversy remains regarding whether PANDAS differs enough from pediatric OCD or tic disorders and other neuropsychiatric disorders to warrant a different diagnostic category (Kronenberg and Shouldice, 2019; Pichichero et al. 2023). The body of research related to PANDAS and PANS is small (number of studies and sample sizes among studies) compared with many other diseases and conditions (see the Medical Effectiveness section).
### Symptoms

Both PANDAS and PANS are characterized by a child experiencing sudden onset or significant worsening of OCD\(^{33}\) and/or tic disorders\(^{34}\) along with at least two additional physical or neuropsychiatric symptoms (Pichichero et al. 2023). OCD symptoms associated with PANDAS may be more abrupt and more extreme than the symptoms of a child diagnosed solely with typical OCD (NIMH, 2019; Rosenberg et al., 2022). Children may also become moody or irritable, or experience anxiety attacks, separation anxiety, rage, fatigue, phobias, insomnia, joint or muscle pain, or eating disorders. Figure 1 describes the intersection and differences between common symptoms for PANDAS/PANS.

**Figure 1. Common Symptoms of PANDAS/PANS Used for Clinical Diagnosis**

The PANDAS Physicians Network\(^{35}\) (PPN, 2023b) classifies cases as:

- **Mild:** Symptoms are significant and last a few hours per day and cause disruptions at home, school or in the community.

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\(^{33}\) OCD includes obsessive thoughts and compulsive behaviors used in an attempt to rid a person of their uncontrolled and distressing thoughts, images, or impulses that occur repeatedly. Examples include obsessions with germs, responsibility, death, identity, or religious/moral ideas. Compulsions are exhibited through repetitive behaviors to neutralize the thoughts such as washing hands or cleaning in a specific way, repeating simple actions such as exiting/entering a door, counting, or repeating body movements such as tapping or blinking (IOF, 2023).

\(^{34}\) Tic disorders include Tourette Syndrome and Persistent Tic Disorder. Tics are involuntary, sudden, repetitive physical movements (e.g., blinking) and vocal sounds (e.g., grunting, yelling a certain word) that occur many times a day, nearly daily for more than a year (CDC, 2023).

\(^{35}\) PANDAS Physicians Network is a clinician-oriented organization that created PPN Guidelines for Diagnostics and Therapeutics, provides education and communication to the medical community, and sponsors research for developing diagnostic tests, treatment protocols and a cure for PANDAS/PANS.
• Moderate: Symptoms are distressing and interfere with daily activities. Symptoms occur about 50% to 70% of waking hours.

• Severe: Symptoms are incapacitating, life threatening, or occupy 71% to 100% of waking hours.

The severity and frequency of symptoms for those diagnosed with PANDAS or PANS can range from a single event with milder and/or fewer symptoms that resolve within weeks to months, to a moderate level that follows a remitting–relapsing pattern of moderate and/or more severe symptoms over multiple months or years, to a multiyear course with severely disruptive, unmanaged symptoms. Milder cases may resolve on their own without treatment, whereas other types of cases may respond to medication and cognitive behavioral therapy (CBT) treatments such that symptoms completely resolve or are reduced and become more manageable (Godlewski, et al., 2021; PPN, 2023c).

Prevalence of PANDAS/PANS in the United States

PANDAS/PANS has been primarily described in children between the ages of 3 and 12 years; however, the exact prevalence and age distribution of PANDAS/PANS is unknown. Because OCD is a required symptom for the diagnosis of PANDAS and PANS, it is thought the prevalence can be estimated as a subset of the prevalence of pediatric OCD. Epidemiological research estimates that 0.5% to 5% of children in the United States are affected by OCD (Nazeer et al., 2020; Rosenberg et al., 2022).

In a study of 136 youth with a lifetime diagnosis of OCD, Jaspers-Fayer at al. (2017) estimate that 5% of children with OCD may meet the criteria for PANDAS/PANS, which translates to about 1 PANDAS/PANS case/10,000 children (Jaspers-Fayer et al., 2017). Based on the statewide population of ~7.6 million California children aged 3 to 17 years (KidsData, 2023), CHBRP estimates that fewer than 1,000 California children would be diagnosed with PANDAS/PANS at any time (regardless of insurance status); note this estimate is based on a single study of 136 children with OCD (Jaspers-Fayer et al., 2017).

Research has found that the average age of onset of pediatric OCD ranges from 7.5 to 12.5 years and that more males than females are diagnosed with the disorder (Godlewski et al., 2021). A survey of patients diagnosed with PANS and parents/legal guardians of patients diagnosed with PANS found the average age of onset of PANS symptoms was around 7.5 years old, but the average age of diagnosis was 9.5 years (similar to that of OCD onset). This survey also found that males comprised 64% of patients and on average were significantly younger than female patients (Calaprice et al., 2017).

Clinical Practice Guidelines

CHBRP found clinical practice guidelines from three different organizations; all recognize the syndromes’ range of severity (mild, moderate, severe) and recommend similar, but not perfectly aligned, treatments.

PANDAS/PANS Clinical Research Consortium

The PANDAS/PANS Clinical Research Consortium, developed out of the 2013 PANS Consensus Conference, describes consensus-based treatment options based on severity (mild, moderate-to-severe, and extreme/life-threatening) and symptoms. The group recommended a three-pronged approach to treat underlying infection and inflammation concurrent with treatment of psychiatric and behavioral symptoms. PANS: Part I: Psychiatric and Behavioral Interventions identifies psychoactive medications, psychotherapies (particularly cognitive behavioral therapy), and supportive interventions to treat neuropsychiatric symptoms (Thienemann et al., 2017); Part II: Immunomodulatory Therapies

36 The PANS Consensus Conference convened researchers and clinicians with clinical interest in PANS/PANDAS in May 2013 at Stanford University. The group consisted of clinicians and researchers specializing in several fields of pediatrics with the goals of clarifying the diagnosis of PANS, developing strategies to evaluate suspected PANS cases and to determine research priorities in the field (Chang et al., 2015).
recommends immunomodulatory and/or anti-inflammatory therapies to treat disturbances of the immune system (based on symptom severity and disease trajectory) (Frankovich et al., 2017); and Part III: Antimicrobial Interventions recommends treatments for infection to remove the source of inflammation (Cooperstock et al., 2017). The guidelines also recommend that clinicians frequently evaluate the effectiveness of the patient’s treatments and adjust according to symptom response.

**PANDAS Physician Network**

The Guidelines and Therapeutics Committee of the PANDAS Physician Network developed diagnostic guidelines and treatment guidelines for children with PANDAS/PANS based on recommendations from the 2013 PANS Consensus Conference, PANDAS/PANS Clinical Research Consortium, and ongoing research and clinical experience (PANDAS, 2020). Diagnostic and treatment guidelines for both PANS and PANDAS are categorized by three severity levels: mild, moderate, and severe. Recommended initial treatments for mild cases include use of antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and CBT. For moderate/severe cases, the recommended initial treatment is to consider a longer course of antibiotics, referral to a psychiatrist to help manage symptoms. For severe cases, prescribing high-dose intravenous and/or prolonged steroid treatment with a taper, or at least one round of IVIG treatment should be considered. Patients should be assessed at follow-up visits to see whether symptoms have improved or worsened, to determine whether treatment should be modified (such as restarting or changing antibiotics, prescribing prednisone or NSAIDs if not already tried), and to consider a possible alternative diagnosis. For severe to extreme cases unresponsive to the treatments listed above or with worsening symptoms, plasma exchange, rituximab infusions, or mycophenolate mofetil should be considered (Chang et al., 2015; Swedo et al., 2012).

**Nordic Pediatric Immunopsychiatry Group**

A group of pediatric neurologists, child psychologists, and child psychiatrists from Nordic countries developed clinical guidance on the diagnosis and management of PANS. The general treatment approach is to 1) treat mental health symptoms; 2) treat ongoing verified infections; and 3) treat suspected inflammation. Specific treatments outlined in the guidelines are antibiotics, NSAIDs, steroids, and IVIG (Pfeiffer et al., 2021). The group adopted clinical and diagnostic criteria consistent with recommendations by PANS/PANDAS experts in the United States (Chang et al., 2015; Swedo et al., 2012), but also proposed criteria for defining severe cases of PANS/PANDAS. Similar to the other guidelines, the Nordic group recommended antibiotics and NSAIDs for initial treatment, and to consider steroids and IVIG for more severe cases. However, the Nordic group did not recommend the use of rituximab for treatment (Pfeiffer et al., 2021).

**PANDAS/PANS Diagnosis and Treatment Path**

PANDAS/PANS is uncommon and despite the first publication on the topic occurring in 1998, it remains unfamiliar to much of the clinical community (Swedo et al., 1998). Clinicians commonly involved in diagnosing PANDAS/PANS may include a family physician, pediatrician, pediatric nurse practitioner, pediatric neurologist, pediatric psychiatrist, neurodevelopmental pediatrician, pediatric rheumatologist, and pediatric allergist/immunologist. Despite the wide variety of clinicians listed, many are unfamiliar with the syndromes and how to diagnose or treat them. There are ~10 PANDAS/PANS clinics nationwide with 2 located in California (Stanford and UCLA) (PPN, 2023a).

**Diagnosis**

Due to the lack of diagnostic laboratory or imaging tests specific to PANDAS/PANS, the overlap of symptoms with multiple conditions, the diagnostic process for these syndromes is challenging. The

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37 PANS has no specific diagnostic or billing codes; an ICD-10 code for PANDAS exists, as noted later in this section. AB 907 would require the use of the codes for autoimmune encephalitis (AE) until national billing codes for
PANDAS/PANS diagnostic process relies primarily on a clinical diagnosis in conjunction with laboratory testing to rule out conditions with similar symptoms such as pediatric autoimmune encephalitis, other pediatric infection-triggered autoimmune neuropsychiatric disorders (e.g., childhood acute neuropsychiatric syndromes (CANS), Sydenham chorea, neuropsychiatric lupus, etc.), Tourette syndrome, pediatric OCD, Tumor Necrosis Factor Receptor Associated Periodic Syndrome, and central nervous system vasculitis (Baj et al., 2020; Godlewski et al., 2021; Hutanu et al., 2022). Misdiagnosis and children’s suppression of behaviors during diagnostic visits also make accurate diagnosis challenging.

The clinical diagnosis focuses on a detailed medical history to define sudden onset, possible relation to recent infections, and documentation of current symptoms (Figure 1). To explore the possibility of a recent, unidentified strep infection, the clinician will perform a throat swab culture to check for Group A beta hemolytic strep (GABHS) (NIMH, 2019). Antibodies to GABHS can be detected in a blood test, indicating a prior infection, but a high anti-strep antibody titer result is not a definitive diagnosis alone for PANDAS. Other tests may include blood tests to diagnose other autoimmune conditions or infections, neuroimaging (e.g., magnetic resonance imaging [MRI]), electroencephalogram (EEG), and cerebral spinal fluid testing.

As discussed in the Policy Context section, the language of AB 907 specifies that for billing and diagnostic purposes, PANDAS and PANS must be coded as autoimmune encephalitis until the American Medical Association and the federal Centers for Medicare and Medicaid Services create and assign a specific code or codes for PANDAS and PANS. As of the published date of this report, an ICD-10 code exists for PANDAS as D89.89, which is used for “other specified disorders involving the immune mechanism, not elsewhere classified.” There is no ICD-10 code associated with PANS.

**Treatment of PANDAS/PANS**

Based on the clinical guidelines discussed in the previous subsection, treatment options for PANDAS/PANS depend on the physical and/or neuropsychiatric symptoms experienced by the patient. Treatments recommended by consensus guidelines will vary according to patient case severity and symptomology (see the Medical Effectiveness section for discussion of potential side effects and harms).

**Antibiotics:** Penicillin, azithromycin, or other types of antibiotics may be prescribed to eliminate a bacterial infection such as *Streptococcus* A.

**Nonsteroidal Anti-inflammatory Drugs (NSAIDS):** Nonsteroidal anti-inflammatory drugs, such as ibuprofen or naproxen, treat pain, fever, and reduce inflammation.

**Corticosteroids:** Steroids are prescribed for their anti-inflammatory and immunosuppressive effects.

**Cognitive Behavioral Therapy (CBT):** This therapy focuses on changing thinking patterns (gaining a better understanding of the behavior and motivation of others and using problem-solving skills to cope with difficult situations) and changing behavioral patterns (role playing to prepare for potentially problematic interactions with others and learning to how to calm the mind and body). It can be used to treat depression, anxiety disorders, OCD, eating disorders, and severe mental illness (APA, 2017).

**Psychotropics:** This large class of medications includes antidepressants (including selective serotonin reuptake inhibitors [SSRIs]), anti-anxiety medications (e.g., benzodiazepines), stimulants, and antipsychotics that are used to manage symptoms of depression, anxiety, attention deficit disorder, insomnia, and OCD or eating disorders.

**Intravenous immunoglobulin (IVIG):** This blood-plasma-derived product is Food and Drug administration (FDA)-approved to treat a handful of diseases but has seen growing demand for off-label PANS/PANDAS become available. The symptoms of AE are closely aligned with those of PANS/PANDAS; however, there are more diagnostic tests available to identify AE than PANS/PANDAS (Barbagallo, et al., 2017).
use\textsuperscript{38} to treat autoimmune disorders and neurological diseases. It is part of the immunomodulator family\textsuperscript{39} that suppresses or enhances immune responses through the delivery of human antibodies intravenously in a clinic setting (Ballow and Shehata, 2023). National shortages have been documented due to plasma collection shortages and lengthy, complex manufacturing processes (FDA, 2022; Rhodes, 2021). Published strategies for optimizing limited supplies for patients include lowering doses, delaying treatments, prioritizing based on medical need, and using alternative therapies when those exist (Rhodes, 2021).

**B-cell modulator (rituximab):** Rituximab is an immunoglobulin G1 monoclonal antibody used to treat rheumatoid arthritis, non-Hodgkin lymphoma, and chronic lymphocytic leukemia. Similar to IVIG, it is administered intravenously in a clinic setting.

**Therapeutic plasma exchange:** This process uses a machine to remove patient plasma and separate the blood into its components. It discards the unwanted cells or plasma into a discard container and returns most of the remaining blood to the patient along with replacement fluids and a short-acting anticoagulant, usually citrate (Kaplan and Fridey, 2022).

**Mycophenolate mofetil:** An immunosuppressant drug FDA-approved for use by organ transplant patients to prevent organ rejection. It is also used to treat autoimmune diseases such as lupus, rheumatoid arthritis and Crohn’s disease (American College of Rheumatology, 2023).

### Barriers to Accessing Diagnosis and Treatment of PANDAS/PANS

Barriers for the diagnosis and treatment of PANDAS/PANS include the lack of evidence on effective treatment options. The lack of clinicians familiar with PANDAS and PANS contributes to long distance travel (and associated travel expenses) for families seeking care (O’Dor et al., 2022; Tang et al., 2021). PANDAS/PANS symptoms overlap with symptoms of other conditions, thus the lack of a definitive test and reliance on a differential diagnosis can lead to delayed diagnosis. Misdiagnosis, and children’s suppression of behaviors during assessments are also treatment barriers in PANDAS/PANS (O’Dor et al., 2022; Tang et al., 2021). Treatment for moderate-to-severe PANDAS/PANS generally requires pediatric specialists, and ideally, coordinated care among treating clinicians who may be in different care settings. For patients with mild or moderate cases, weekly therapy with CBT, or outpatient daily therapy may be prescribed, but due to pediatric behavioral health workforce shortages in California (Coffman et al., 2018), both may be difficult to access. For patients with more severe cases, space in inpatient day programs or hospitalizations, where treatment may last from 1 week to months, may be difficult to obtain due to California’s shortage of pediatric psychiatric care clinicians and inpatient and treatment beds (AACAP, 2023; Weiner, 2021).

### Disparities\textsuperscript{40} in PANDAS/PANS

CHBRP found no literature identifying disparities regarding PANDAS/PANS.

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\textsuperscript{38} Off-label use refers to an FDA-approved medication used to treat a condition or symptom that is not approved by the FDA. According to the FDA, once a drug is approved, “healthcare providers generally may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient.” (FDA, 2018). It is common practice among clinicians to prescribe medications off-label.

\textsuperscript{39} Other immunomodulators include corticosteroids and NSAIDs.

\textsuperscript{40} Several competing definitions of “health disparities” exist. CHBRP relies on the following definition: Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population (Wyatt et al., 2016).
Quality of Life

The symptoms associated with PANS/PANDAS can negatively affect family and child quality of life including community and social participation, activities of daily living, and education, and require substantial changes to work and family life routines (Demchick et al., 2019).

Frankovich et al. (2018) measured the longitudinal caregiving burden of children diagnosed with PANDAS/PANS who were treated at the Stanford PANS clinic. During first flares, caregiver burden for half of the study respondents (48 of 97 respondents) was high enough to indicate an increased need for respite care, scoring above similar studies of caregivers of Alzheimer’s patients. Over a three-year follow-up, Frankovich et al. reported an overall reduction in caregiver burden regardless of continued affiliation with the clinic. The study reported that delays in treatment initiation did not affect the rate of change in caregiver burden.
MEDICAL EFFECTIVENESS

As discussed in the Policy Context section, AB 907, as amended March 16, 2023, would mandate coverage of prophylaxis, diagnosis, and certain treatments for Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). The treatments covered under this bill would include the following:

- Antibiotics;
- Medication and behavioral therapies to manage neuropsychiatric symptoms;
- Immunomodulating medicines;
- Plasma exchange; and
- Intravenous immunoglobulin therapy (IVIG).

The medical effectiveness review summarizes findings from evidence on these treatments and their effectiveness in reducing or eliminating symptoms of PANDAS/PANS. Symptoms are broad and differ by case, however the most common symptoms include obsessive-compulsive disorder (OCD), tics, and eating restrictions. Additional information on these treatments and syndromes are included in the Background on PANDAS and PANS section.

Research Approach and Methods

CHBRP relied on a systematic review on treatment of PANDAS/PANS published in 2018 for findings from studies published prior to 2017 (Sigra et al., 2018). For the period 2017 and following, CHBRP conducted a supplemental review of abstracts of studies published in English from 2017 to present. This supplemental review yielded 129 articles as candidates for the analysis.

Of the 129 articles found in the supplemental literature review, 14 were considered for full text review, of which two were ultimately included for the medical effectiveness review. Combined with the nine studies identified between two systematic reviews (Johnson et al., 2021; Sigra et al., 2018), a total of 11 studies were included in the medical effectiveness review.

CHBRP found research available for PANDAS and PANS to be very limited; studies, when available, were sparse and conducted with very small sample sizes. Because of the very limited evidence, a few observational studies lacking comparison groups were included when no rigorous evidence was available. Of note, eight of the nine studies from the systematic reviews were assessed to have a high or moderate risk of bias.

The other articles were eliminated because they did not focus on pediatric patients diagnosed with PANDAS/PANS, were of poor quality, or did not report findings from clinical research studies. A more thorough description of the methods used to conduct the medical effectiveness review and the process used to grade the evidence for each outcome measure is presented in Appendix B.

The conclusions below are based on the best available evidence from peer-reviewed and grey literature. Unpublished studies are not reviewed because the results of such studies, if they exist, cannot be obtained within the 60-day timeframe for CHBRP reports.

41 Much of the discussion in this section is focused on reviews of available literature. However, as noted in the section on Implementing the Hierarchy of Evidence in the Medical Effectiveness Analysis and Research Approach document (posted at www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis in the absence of fully applicable to the analysis peer-reviewed literature on well-designed randomized controlled trials (RCTs), CHBRP’s hierarchy of evidence allows for the inclusion of other evidence.

42 Grey literature consists of material that is not published commercially or indexed systematically in bibliographic databases. For more information on CHBRP’s use of grey literature, visit www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.
Key Questions

1. For children experiencing PANDAS/PANS, what is the effectiveness of antibiotics in reducing or eliminating symptoms? What are the harms?

2. For children experiencing PANDAS/PANS, what is the effectiveness of behavioral therapies and psychotropic medications in reducing or eliminating symptoms? What are the harms?

3. For children experiencing PANDAS/PANS, what is the effectiveness of immunomodulating treatments (e.g., NSAIDs, corticosteroids, IVIG, plasma exchange, rituximab, mycophenolate mofetil, and vitamin D) in reducing or eliminating symptoms? What are the harms?

Methodological Considerations

As described in the Background on PANDAS and PANS section, PANDAS and PANS are both rare syndromes with an episodic course, in which patients may experience a broad range of symptoms with varying levels of severity.

There is no specific diagnostic test to confirm a diagnosis for PANDAS or PANS, and other conditions may present with similar symptoms, making it difficult to reliably diagnose and study PANDAS/PANS. Clinicians use a differential diagnostic process that may include collecting a patient’s medical history or conducting blood tests to rule out other conditions that may cause similar symptoms. Additional tests may include testing for Group A Streptococcus, or Mycoplasma pneumoniae – infections that may be associated with PANDAS or PANS (Chang et al., 2015; Pfeiffer et al., 2021b). The evidence for the use of tests for diagnosis of other conditions or for PANDAS/PANS associated infections is beyond the scope of what CHBRP is able to review within the legislative timeline.

As described in the Policy Context section, AB 907 would require that “coverage for PANDAS and PANS shall adhere to the treatment recommendations developed by a consortium of medical professionals convened to research, identify, and publish clinical practice guidelines and evidence-based standards for the diagnosis and treatment of those disorders.” CHBRP identified 3 clinical practice guidelines that meet the above criteria for diagnosing and treating patients with PANDAS/PANS (Chang et al., 2015; Cooperstock et al., 2017; Frankovich et al., 2017; Pfeiffer et al., 2021b; Thienemann et al., 2017). The treatment modalities recommended in these guidelines were assessed by CHBRP via rapid evidence review for medical effectiveness in reducing or eliminating symptoms of PANDAS/PANS, and for possible harms of these treatments. CHBRP also included information on known side effects of these treatment modalities for other conditions in the pediatric population for additional context.

Outcomes Assessed

For studies of the impact of AB 907, CHBRP assessed effects on two outcomes: (1) reduction or elimination of symptoms associated with PANDAS/PANS (e.g., OCD, tics, anxiety, irritability, or eating disorders); and (2) harms associated with the treatments.

Study Findings

This following section summarizes CHBRP’s findings regarding the strength of evidence for the effectiveness of antibiotics, psychotropic medications, behavioral therapy, plasma exchange, intravenous immunoglobulin therapy (IVIG) and other immunomodulating medications addressed by AB 907, specifically, for children affected by PANDAS/PANS. Each section is accompanied by a corresponding figure. The title of the figure indicates the treatment for which evidence is summarized. The statement in the box above the figure presents CHBRP’s conclusion regarding the strength of evidence about the
effect of a particular treatment based on a specific relevant outcome and the number of studies on which CHBRP’s conclusion is based. Definitions of CHBRP’s grading scale terms are included in the box below, and more information is included in Appendix B.

The following terms are used to characterize the body of evidence regarding an outcome:

**Clear and convincing evidence** indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

*Preponderance of evidence* indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

*Limited evidence* indicates that the studies have limited generalizability to the population of interest and/or the studies have a fatal flaw in research design or implementation.

*Inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

*Insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

More information is available in Appendix B.

**Findings on the Effectiveness and Harms of Antibiotics in Reducing or Eliminating Symptoms for Children With PANDAS/PANS**

Two systematic reviews (Johnson et al., 2021; Sigra et al., 2018) found three studies, all with moderate risk of bias, (two randomized controlled trials [RCTs] and one cross-over RCT) assessing antibiotics as a treatment option for children with PANDAS/PANS. The supplemental literature search did not identify any additional studies.

**Antibiotics for reducing or eliminating symptoms**

One double-blind RCT (Murphy et al., 2017) assigned 31 children with PANS to receive azithromycin or placebo (17 azithromycin, 14 placebo) for 4 weeks and a twice daily probiotic. Patients were recruited online and from the University of South Florida Rothman Center Pediatric Neuropsychiatry, and were included in the study if they met inclusion criteria (acute onset or relapse within 6 months of evaluation, experienced OCD symptoms as measured on the Children’s Yale-Brown Obsessive Compulsive Scale, scored moderate to high on the Clinical Global Impression Severity, had at least two co-occurring neuropsychiatric symptoms [anxiety, emotional lability, tics, frequent urination, or food restrictive symptoms], were aged 4 to 14 years, and were either on a stable dose of neuropsychiatric medication or were not taking any). Participants were not tested for any active infections, but the authors assumed that some participants in the group would have a Group A Strep or Mycoplasma infection. The small study’s results found a significant treatment effect for the azithromycin group in one measure used to assess OCD severity symptoms (OCD-Clinical Global Impressions Scale: seven participants [41.2%] vs. one [7.2%] met treatment responder criteria at week 4; p = 0.045). In another measure for OCD severity (Children’s Yale-Brown Obsessive Compulsive Scale) findings were not statistically significant; the average reduction was 30.5% in the azithromycin group, and 17.2% in the placebo group (p = 0.258). Tic severity also declined in both groups, showing no significant difference between groups on the Yale Global Tic Severity Scale (p = 0.667), or the tic subscale of the Clinical Global Impression – Severity Scale (p = 0.257).
Prophylactic use of antibiotics

In a double-blind cross-over RCT, (Garvey et al., 1999) compared penicillin (250 mg, taken twice daily) against a placebo with the intention of reducing neuropsychiatric exacerbations by preventing future streptococcal infections. 37 children with PANDAS were randomized to receive either 4 months of penicillin, followed by 4 months of placebo (n = 19), or 4 months of placebo, followed by 4 months of penicillin (n = 18). Children were included in the study if they met DSM-III-R or DSM-IV criteria for a tic and/or obsessive-compulsive disorder, had a history of sudden onset of symptoms that developed prior to puberty, were aged 4 to 15 years, and had evidence of an association between streptococcal infections and onset or exacerbations of symptoms. There was no limit on time since the onset of symptoms to be eligible for participation. Children were excluded if tic or OCD severity required hospitalization, or if they had a diagnosis of autism, pervasive developmental delay, mental retardation, other neurologic diagnoses, or severe, comorbid psychiatric disorders. The authors found no significant differences in the number of streptococcal infections between the two groups (14 in penicillin group, 21 in placebo), nor was there a significant difference between groups in OCD severity (as measured by the (Children’s Yale-Brown Obsessive Compulsive Scale), or tic severity (as measured by the Yale Global Tic Severity Scale).

Another double-blind RCT (Snider et al., 2005) of 23 children diagnosed with PANDAS examined the prophylactic use of antibiotics on future streptococcal infections and neuropsychiatric exacerbations. Children were included in the study if they met DSM-IV criteria for a tic and/or obsessive-compulsive disorder, had a history of sudden onset of symptoms that developed prior to puberty, and had evidence of an association between streptococcal infections and onset or exacerbations of symptoms. Participants were tested via throat culture to ensure no active streptococcal infection was present and were randomized to receive either penicillin (n = 11; 250 mg, taken twice daily), or azithromycin (n = 12; 250 mg, taken two times on 1 day of the week, with placebo 6 days a week) for 12 months. 23 out of 24 participants who started treatment completed the full length of the study. Streptococcal infections were documented by review of medical records for the prior year to establish a baseline with a mean of 1.9 infection in the penicillin group and 2.4 infections in the azithromycin group. Participants in both groups experienced fewer streptococcal infections during the study, compared to the streptococcal infections documented in their medical records the year before (mean of 0.1, two total infections – one in each group.) The study also reported significantly fewer neuropsychiatric exacerbations compared to the baseline year, though these exacerbations were not well defined by the authors. Overall, the study found no difference in the number of streptococcal infections or neuropsychiatric exacerbations between patients receiving azithromycin and those receiving penicillin for 12 months.

Potential Harms from Antibiotic Use

Adverse effects reported in the Murphy study (2017) were higher for the azithromycin group and included loose stools (52.94% in the treatment group, 7.14% in the placebo group). Four participants in the azithromycin group had borderline prolonged QTc intervals on ECG from 440 to 460 milliseconds (ms) at the end of week 4 (414.56 ms, SD = ±19.39 ms), two of whom had a prolonged QTc at baseline. Adverse effects were not reported in Garvey et al. (1999) or Snider et al. (2005). Studies of use of antibiotics for other conditions in children have documented nausea, vomiting, abdominal pain, Clostridium difficile (C. diff) infection, skin rash, hives, and anaphylaxis (Butler et al., 2022). Long-term antibiotic use can contribute to antibiotic resistance.

43 A prolonged QTc or “long QT” indicates unusual electrical activity in the heart’s ventricles, as measured by an electrocardiogram (EKG). Symptoms can include fainting during stress or exercise, gasping while sleeping, deafness, muscle weakness, behavioral concerns, learning, memory, seizures, cardiac arrest, or sudden death (NIH, 2022). Before puberty, a QTc <450 ms is considered normal, between 450 and 459 borderline, and ≥460 prolonged. After puberty in males, a QTc between 460 and 469 is borderline and ≥470 is considered prolonged. In post-pubertal females, 460 to 479 is borderline and ≥480 ms is considered prolonged (Berul, 2022).
Summary of findings regarding antibiotic treatment or prophylaxis for patients with PANDAS/PANS: There is inconclusive evidence based one systematic review including three small clinical trials involving a total of 89 participants that antibiotics used for treatment or prophylaxis are effective in reducing or eliminating symptoms with PANDAS/PANS.

Figure 2. Effectiveness of Antibiotics for Patients With PANDAS/PANS

Findings on the Effectiveness of Behavioral Therapies and Psychotropic Medications in Reducing or Eliminating Symptoms for Children With PANDAS/PANS

One systematic review (Sigra et al., 2018) found two nonrandomized studies without concurrent comparison groups that investigated the effect of cognitive behavioral therapy (CBT) on psychological symptoms for patients with PANDAS/PANS. Both studies had a high risk of bias due to a lack of randomization or blinding, and high attrition. The supplemental literature search did not identify any additional studies. The waitlist-controlled trial (Storch et al., 2006) (seven participants) involved 14 CBT sessions that occurred over the span of 3 weeks. Six of seven participants demonstrated significant reductions in OCD symptoms (as measured by the Children’s Yale-Brown Obsessive Compulsive Scale) but experienced no change in depression or anxiety symptoms.

In an uncontrolled trial, (Nadeau et al., 2015), eight participants with PANS completed 14 CBT sessions on a twice-weekly schedule, and six were available for the final follow-up assessment. Participants who completed the study experienced reductions in OCD symptoms (as measured by the Children’s Yale-Brown Obsessive Compulsive Scale), but no changes in anxiety symptoms. The studies did not report any harms or adverse events. The authors of the systematic review concluded that although CBT is an evidence-based treatment for patients with OCD, it has not been sufficiently studied in patients with PANDAS/PANS in a controlled setting. Thus, the evidence for CBT in reducing or eliminating OCD symptoms for patients with PANDAS/PANS is insufficient.

CHBRP did not find any trials involving the use of psychotropic medications for use with pediatric patients with PANDAS/PANS. A survey study found that SSRIs, antipsychotics, attention-deficit/hyperactivity disorder (ADHD) medications, anxiolytics, and mood-stabilizing medications are widely prescribed for children diagnosed with PANDAS/PANS (Calaprice et al., 2018).

Potential harms from CBT and psychotropic use

Harms of CBT for treatment of OCD or depression in children are considered minimal, though comparative evidence on harms is limited (Uhre et al., 2020; Viswanathan et al., 2020). A systematic review and meta-analysis of the use of selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) for all indications found a two-fold increase in rates of suicidality and aggressive behavior in children and adolescents (Sharma et al., 2016). Another largescale systematic review on adverse events reported in children using psychotropics found additional harms (Solmi et al., 2020). Adverse events for antidepressants include nausea/vomiting, sedation, diarrhea, headache, weight gain or loss, anorexia, and extrapyramidal symptoms. For antipsychotics, adverse

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44 SNRIs are medications that are FDA-approved to treat depression symptoms, as well as other conditions such as fibromyalgia and generalized anxiety disorder.

45 Extrapyramidal symptoms include a broad range of drug-induced movement disorders and can include involuntary muscle contractions, abnormal posturing, or repetitive movements. These movements can occur in many areas of the
events varied by type and include weight gain, extrapyramidal symptoms, increased cholesterol, and elevated glucose levels/diabetes. Medications for ADHD have some reported adverse events, including abdominal pain, sedation, anorexia, insomnia, hypertension and prolonged QTc. Adverse events for mood stabilizers also varied by type, and include sedation, nausea/vomiting, weight gain, weight loss, low blood platelet count, and low white blood cell count.

Summary of findings regarding CBT and psychotropic medications for patients with PANDAS/PANS: There is insufficient evidence that CBT is effective in reducing or eliminating OCD symptoms for patients with PANDAS/PANS based on two very small studies identified in one systematic review involving a total of 15 participants. There is insufficient evidence on the effectiveness of psychotropic medications for reducing or eliminating behavioral symptoms for pediatric patients with PANDAS/PANS as no published studies were identified.

Figure 3. Effectiveness of CBT for Patients With PANDAS/PANS

Figure 4. Effectiveness of Psychotropics for Patients With PANDAS/PANS

Findings on the Effectiveness of Immunomodulating Therapies in Reducing or Eliminating Symptoms for Children with PANDAS/PANS

Nonsteroidal anti-inflammatory drugs (NSAIDs)

The two systematic reviews (Johnson et al., 2021; Sigra et al., 2018) did not identify any clinical trials testing the use of NSAIDs in pediatric patients with PANDAS/PANS. The supplemental literature search identified one retrospective observational study with no comparison group. The study (Brown et al., 2017b) used electronic medical records from the Stanford PANS Clinic to describe the effects of NSAID use on PANDAS/PANS flares (defined as an acute neuropsychiatric deterioration). Eligible patients included those followed in the clinic who met PANS diagnostic criteria, as defined by Chang (Chang et al., 2015), had at least one documented flare, and had adequate documentation to assess flare duration. Patients who demonstrated no reduction in symptoms after their initial evaluation in the clinic, or who required more aggressive treatment to achieve their baseline functioning were excluded from the study. Patients who did not start NSAID treatment for a flare until more than 30 days after it started, or who had received treatment with IVIG, high dose IV methylprednisolone, or plasma exchange within the past 50 days were also excluded. The final group included 95 patients and 390 flares and included patients on prophylactic NSAIDs (used before onset of a flare) and NSAID treatment started within 30 days after the flare. NSAIDs included ibuprofen, naproxen, sulindac, and celecoxib. Although most flares were not treated with NSAIDs, the study found that treatment after the flare symptoms began or prophylactic use of NSAIDs were associated with a shorter flare duration than flares not treated with NSAIDs (prophylactic NSAID difference 4 weeks, (95% CI [1.85-6.24]; p < 0.01; early NSAID use difference 2.5 weeks (95% CI

body, including the back, neck, jaw, eyes, abdominal wall and pelvic muscle, facial and tongue muscles, and extremities (D’Souza and Hooten, 2023).
It also found that flare duration did not differ significantly between NSAIDs used prophylactically or prescribed within 30 days of flare onset \(p = 0.26\).

**Potential Harms of NSAIDs**

Participants in the Brown study experienced side effects including abdominal pain (5), skin rash (1), bruising (1), high levels of protein in urine (3), and clinically insignificant elevated liver enzymes (1). Long term or chronic use of NSAIDs can adversely affect the digestive, renal, cardiovascular, hepatic, and/or hematologic systems (Ghlichloo and Gerriets, 2022).

<table>
<thead>
<tr>
<th>Summary of findings regarding NSAIDs for patients with PANDAS/PANS:</th>
<th>There is insufficient evidence that NSAIDs are effective in reducing or eliminating symptoms for patients with PANDAS/PANS based on a lack of evidence (no controlled clinical trials and 1 retrospective observational study without a comparison group).</th>
</tr>
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**Corticosteroids**

The two systematic reviews (Johnson et al., 2021; Sigra et al., 2018) did not identify any clinical trials evaluating the use of oral corticosteroids in pediatric patients with PANDAS/PANS. The supplemental literature search identified 1 retrospective observational study with no comparison group on the use of oral corticosteroids on children having PANDAS/PANS flares (Brown et al., 2017a). The investigators reviewed electronic medical records from the Stanford PANS Clinic to identify eligible patients who met PANS or PANDAS research diagnostic criteria (Chang et al., 2015; Swedo et al., 1998, 2012) and who had been treated with steroids during an initial episode or a subsequent flare of symptoms. Patients who required more aggressive treatment to alleviate symptoms were excluded from the study, including aggressive disease-modifying treatments such as chronic use of IVIG or high dose IV methylprednisolone, as were patients whose records did not document the duration of the flare. The final group included 98 patients (403 flares), 54 of whom (85 flares) had received treatment with corticosteroids. The study found that children treated with corticosteroids experienced a shorter flare duration \(6.4 \pm 1.5\) weeks than those not treated with corticosteroids \((11.4 \pm 8.6\) weeks \(p < 0.001\)). In a multilevel model adjusted for demographics, disease and treatment variables, use of oral corticosteroids was associated with flares that were 3.5 weeks shorter \(95\% CI [1.10-5.95]\).

**Potential Harms From Corticosteroid Use**

Temporary side effects were reported for 44% of 102 corticosteroid courses, including escalation of symptoms: OCD symptoms (10), anxiety (16), emotional lability/moodiness (12), irritability/agitation (15), sleep disturbance (10), tics (7), aggression/anger/rage (4), urinary symptoms (5), mania (3), sensory amplification (3), hyperactivity (2), hallucinations (2), vision abnormalities (2), behavior regression (2), and flat affect (1). In 3 patients, steroids were stopped due to worsened neuropsychiatric symptoms. Of the 15 patients who received a corticosteroid course for >5 days, or more than 3 courses within 1 month, 2 experienced weight gain, 4 experienced weight gain and Cushingoid features, 46 and 2 experienced only Cushingoid features. Adverse effects noted from treatment of other conditions are seen in up to 90% of

\[0.43-4.68\]; \(p < 0.02\).
patients who take corticosteroids for more than 60 days and include suppression of the hypothalamic-pituitary-adrenal (HPA) axis, Cushingoid features, diabetes and hyperglycemia, myopathy, psychiatric disturbances, immunosuppression, cardiovascular disease, and effects on gastrointestinal and skin and bones (Hodgens and Sharman, 2022).

**Summary of findings regarding corticosteroids for patients with PANDAS/PANS:** There is insufficient evidence that oral corticosteroids are effective on reducing symptoms for patients with PANDAS/PANS based on a lack of controlled clinical trials and a single retrospective observation study with no comparison group. CHBRP did not find any studies on the use of intravenous corticosteroids for patients with PANDAS/PANS.

**Figure 6. Effectiveness of Corticosteroids for Patients With PANDAS/PANS**

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<thead>
<tr>
<th>NOT EFFECTIVE</th>
<th>INSUFFICIENT EVIDENCE</th>
<th>EFFECTIVE</th>
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<tbody>
<tr>
<td>Clear and Convincing</td>
<td>Limited</td>
<td>Preponderance</td>
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<tr>
<td>Preponderance</td>
<td>Inconclusive</td>
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<tr>
<td>Limited</td>
<td>Preponderance</td>
<td>Clear and Convincing</td>
</tr>
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</table>

**Intravenous immunoglobulin (IVIG)**

Both systematic reviews (Johnson et al., 2021; Sigra et al., 2018) identified two small clinical trials (Perlmutter et al., 1999; Williams et al., 2016) testing the use of IVIG for treating OCD and tic symptoms in patients with PANDAS/PANS among a total of 63 patients. The supplemental search identified two additional small uncontrolled studies (Hajjari et al., 2022; Melamed et al., 2021) describing a total of 31 patients.

In the Perlmutter trial, 29 patients were randomized to receive IVIG, placebo, or plasma exchange. To meet eligibility criteria, patients had to meet DSM-III criteria for a tic and/or OCD disorder, experienced a sudden onset (or episodic course) of neuropsychiatric symptoms before puberty, evidence of an association between streptococcal infection and onset or exacerbation of signs and symptoms, and current exacerbation severe enough to cause significant distress and interfere with child’s home, school, and/or social relations. Patients were excluded if they had a history of Sydenham’s chorea, rheumatic fever, autism, schizophrenia or other psychotic or neurological disorder, an autoimmune disorder, or other medical illness. Nine patients were randomized into the IVIG group, five of whom were taking some type of psychotropic at the time of treatment (three SSRIs, one SSRI + another antidepressant, and one neuroleptic + SSRI). 10 patients were randomized into the placebo group, for which 5 were also taking some type of psychotropic at the time of treatment (two SSRIs, three SSRI + another antidepressant, and one neuroleptic). Participants who were randomized into the IVIG or placebo (saline solution given in the same manner as IVIG) groups were blind to their treatment, however, those receiving plasma exchange were not blinded. The IVIG and placebo groups received 2 consecutive days of treatment (IVIG at 1g/kg dose). At 1 month follow-up, OCD symptoms (as measured by the Children’s Yale-Brown Obsessive Compulsive Scale) in the IVIG group showed greater reductions compared to the placebo group (45% reduction for IVIG group, 3% reduction for placebo group). Both the IVIG and placebo groups demonstrated a similar reduction in tic symptoms (as measured by the Tourette Syndrome Unified Rating Scale) (19% reduction for IVIG group, 12% reduction for placebo group). The Williams trial (35 patients) used a similar study design to Perlmutter but found no significant difference in reduction of OCD symptoms (as measured by the same Obsessive-Compulsive Scale) between the IVIG group and the placebo at 6-week follow-up (22% reduction for IVIG group, 11% reduction for placebo group).

An uncontrolled study (Melamed et al., 2021) provided all 21 participants with IVIG treatment at 1g/kg every 21 days, over a period of 18 weeks (six infusions). Eligibility criteria included age 4 to 16 years, diagnosed with moderate to severe PANS that was confirmed via parent questionnaire (PANS Scale –
Parent Version), with symptoms that were unresponsive to prior treatments. Participants were excluded if they had a history of rheumatic fever or Sydenham’s chorea, previous IVIG therapy within 6 months of screening, or use of corticosteroids within 6 weeks of screening. At 26-week follow-up, OCD symptoms (as measured by the Children’s Yale-Brown Obsessive Compulsive Scale) reduced from a baseline mean of 22.10, to 8.52. At the same timepoint, tic symptoms (as measured by the Yale Global Tic Severity Scale) had reduced from a baseline mean of 36.81, to 12.29.

A second uncontrolled study (Hajjari et al., 2022) provided 10 children with a pre-existing diagnosis of post-infectious PANDAS/PANS, with 2g/kg IVIG treatment once/month for 3 months. Eligibility criteria included aged 4 to 17 years, diagnosed with post-infectious PANDAS/PANS (using criteria from Swedo et al., 2012), and no use of IVIG within the past 6 months. Exclusion criteria included having an acute or chronic disease that would put the patient at risk, history of serious reactions to blood-derived products, pregnancy, kidney disease, taking medications with immunosuppressants, immunomodulators, or long-term corticosteroid use, history of drug abuse, subjects/families who could not provide independent informed consent, or participation in another clinical trial within past 30 days. Six of the 10 participants had pre-existing diagnosed or suspected neurodevelopmental disorders including autism, ADHD, and epilepsy. The study reported on OCD symptoms (using the Children’s Yale-Brown Obsessive Compulsive Scale) and found a nonsignificant reduction in mean scores from baseline to 4 months later (M = 24, SD, 7.80. M = 17.8, SD, 7.67; p = 0.005). The PANS Scale, a scale that rates severity of 12 possible symptoms from “Absent” to “Extreme” and is calculated to form a composite score, was completed via interview with the patient and parent. Mean scores for the scale declined by 33% after 1 month (81.2% to 54.0%), however the effect was global, with no specific symptom improvement.

Potential Harms From IVIG Use

Adverse events were common with IVIG but generally transient. In the Perlmutter trial, 6 of the 9 children who received IVIG experienced adverse effects including nausea/vomiting (5), headache (3), and fever (4). Two of the 10 children in the placebo group experienced nausea/vomiting, and 1 experienced a headache. In the Williams trial, adverse effects included headache, sore throat, nausea/vomiting, muscle/bone/joint pain, fatigue, and anxiety. Adverse effects in the Melamed study (2021) included headache, nausea/vomiting, and rash. In the Hajjari study, adverse effects included headache, neck and/or pain, nausea, vomiting, irritability, and fatigue. One child developed temporary anemia, and another experienced a brief allergic reaction. Aseptic meningitis has also been identified as another common side effect of IVIG infusion (Cooperstock et al. 2017).

| Summary of findings regarding IVIG for patients with PANDAS/PANS: There is inconclusive evidence from 2 small, controlled studies with conflicting evidence, and 2 small, uncontrolled studies involving 95 participants in total, that IVIG is effective in reducing tic and/or OCD symptoms for patients with PANDAS/PANS. |

Figure 7. Effectiveness of IVIG for Patients With PANDAS/PANS
**Therapeutic plasma exchange**

Both systematic reviews (Johnson et al., 2021; Sigra et al., 2018) identified 1 small trial (Perlmutter et al., 1999) testing the use of plasma exchange on alternate days for five to six treatments over 10 to 12 days in pediatric patients with PANDAS/PANS. The supplemental literature search did not identify any additional studies. In the Perlmutter trial, 29 patients were randomized to receive IVIG, placebo (simulating the IVIG infusion process), or plasma exchange. Ten participants were randomized into the plasma exchange group; of these, 7 patients were taking some type of psychotropic at the time of treatment (two were taking SSRIs, two neuroleptics, and three were taking a neuroleptic and SSRI). Due to the design of the study and the nature of the treatment (patients must be connected by IV to a plasmapheresis machine for 1 to 2 hours), patients who received the plasma exchange treatment were aware that they were receiving that intervention. At 1-month follow-up, OCD symptoms (as measured by the Children’s Yale-Brown Obsessive Compulsive Scale) for the plasma exchange group decreased from an average 22.5 at baseline to an average of 9.5 (p < 0.05), a statistically significant difference. For tic symptoms (as measured by the Tourette Syndrome Unified Rating Scale), the plasma exchange group experienced a statistically significant decrease from an average of 21.7 to 11.0 (p < 0.05). Additional results on global impairment and severity were provided, however, these scales were not adequately described.

**Potential Harms From Plasma Exchange Use**

Adverse effects for the plasma exchange group in the Perlmutter trial (1999) included pallor, dizziness, nausea, vomiting, and anxiety. Additional possible complications of plasma exchange include reduction in serum calcium or potassium with related symptoms including paresthesia, tetany, and arrhythmias. Anaphylaxis may also occur (Kaplan and Fridey, 2022).

**Summary of findings regarding plasma exchange for patients with PANDAS/PANS:** There is insufficient evidence from 1 trial of 10 patients that plasma exchange is effective on reducing symptoms for patients with PANDAS/PANS based on a lack of controlled clinical trials.

**Figure 8. Effectiveness of Plasma exchange for Patients With PANDAS/PANS**

**Rituximab**

CHBRP did not find any studies involving the use of rituximab for pediatric patients with PANDAS/PANS.

**Potential Harms From Rituximab Use**

Possible side effects for rituximab can include fever, headache, rash, fatigue, infection, hemolysis or other hemolytic reactions, anaphylaxis, renal failure, thrombosis, dermatological reactions, neutropenia, lung injury, seizures, and death (Frankovich et al., 2017; Lexicomp, 2023).

**Summary of findings regarding rituximab for patients with PANDAS/PANS:** There is insufficient evidence that rituximab is effective on reducing symptoms for patients with PANDAS/PANS based on a lack of controlled clinical trials or other studies.
**Mycophenolate mofetil**

CHBRP did not find any studies involving the use of mycophenolate mofetil for pediatric patients with PANDAS/PANS.

**Possible Harms From Mycophenolate Mofetil Use**

Possible side effects of mycophenolate mofetil can include sensory disturbances, cytopenia, dizziness, nausea, diarrhea, abdominal pain, dermatologic reactions, hemolytic reactions, abnormal renal or hepatic function, malignant neoplasms, increased risk of sepsis or other infections, including CMV (cytomegalovirus), herpes zoster, BK virus, hepatitis B, and hepatitis C (Frankovich et al., 2017).

**Summary of findings regarding mycophenolate mofetil for patients with PANDAS/PANS:** There is insufficient evidence that mycophenolate mofetil is effective on reducing symptoms for patients with PANDAS/PANS based on a lack of controlled clinical trials.

**Vitamin D**

CHBRP did not find any studies involving the use of vitamin D for pediatric patients with PANDAS/PANS.

**Summary of findings regarding vitamin D for patients with PANDAS/PANS:** There is insufficient evidence that vitamin D is effective on reducing symptoms for patients with PANDAS/PANS based on a lack of controlled clinical trials.

**Summary of Findings**

Table 3 summarizes evidence of the effectiveness of antibiotics, behavioral therapies, psychotropics, NSAIDs, corticosteroids, IVIG, plasma exchange, rituximab, mycophenolate mofetil, and vitamin D on reducing or eliminating symptoms for pediatric patients with PANDAS/PANS. Evidence is reported separately for: (1) the treatment’s effectiveness at reducing or eliminating symptoms of PANDAS/PANS; and (2) reported harms associated with the treatment. Overall, the evidence is insufficient or inconclusive.
that any of these treatments are effective at reducing prominent symptoms, such as OCD symptoms, tics, or eating restrictions, for pediatric patients with PANDAS/PANS. As stated in the introduction, research available for PANDAS/PANS is very limited; studies are few, small, and demonstrate moderate to high levels of bias. This analysis included a total of approximately 394 individual participants though this number is likely an overestimate due to probable overlap of the patient populations described in the Brown et al., 2017 (95 patients) and Brown et al., 2017a (98 patients) studies. Additional studies involving controlled clinical trials, larger sample sizes, and clear eligibility criteria are necessary to determine which treatments are effective for children with PANDAS/PANS.

### Table 3. Summary of Evidence of Medical Effectiveness of Test/Treatment/Service

<table>
<thead>
<tr>
<th>Type of Treatment</th>
<th>Evidence Level for Reducing or Eliminating Symptoms of PANDAS/PANS</th>
<th>Evidence of Possible Harms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Inconclusive evidence</td>
<td>Side effects can include loose stools, and prolonged QTc. Studies of use of antibiotics for other conditions in children have documented nausea, vomiting, abdominal pain, C. diff infection, skin rash, hives, and anaphylaxis. Long term antibiotic use can contribute to antibiotic resistance.</td>
</tr>
<tr>
<td>Behavioral therapy (CBT)</td>
<td>Insufficient evidence</td>
<td>Insufficient evidence.</td>
</tr>
<tr>
<td>Psychotropics</td>
<td>Insufficient evidence</td>
<td>Antidepressants: nausea/vomiting, headache, diarrhea, sedation, weight gain or loss, extrapyramidal symptoms(^{47}), anorexia, aggression, and suicidality. Antipsychotics: weight gain, extrapyramidal symptoms, increased cholesterol, and elevated glucose levels/diabetes. ADHD medications: abdominal pain, sedation, anorexia, insomnia, hypertension, and prolonged QTc(^{48}). Mood stabilizers: nausea/vomiting, sedation, weight gain, weight loss, low blood platelet count, and low white blood cell count.</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Insufficient evidence</td>
<td>Abdominal pain, skin rash, bruising, proteinuria, and clinically insignificant transaminits. Long term use can affect the digestive, renal, cardiovascular, hepatic, and/or hematologic systems.</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Insufficient evidence</td>
<td>Psychiatric adverse effects can include escalation of symptoms including OCD symptoms, anxiety, emotional lability/moodiness, irritability/agitation, sleep disturbance, tics, aggression/anger/rage, urinary symptoms, mania, sensory amplification, hyperactivity, hallucinations, vision abnormalities, behavior regression, and flat affect. Other adverse effects can include weight gain, Cushingoid features, hyperglycemia, diabetes, myopathy, psychiatric disturbances, immunosuppression, cardiovascular disease, and effects on gastrointestinal tract, skin, and bone.</td>
</tr>
</tbody>
</table>

\(^{47}\) Extrapyramidal symptoms include a broad range of drug-induced movement disorders and can include involuntary muscle contractions, abnormal posturing, or repetitive movements. These movements can occur in many areas of the body, including the back, neck, jaw, eyes, abdominal wall and pelvic muscle, facial and tongue muscles, and extremities (D'Souza and Hooten, 2023).

\(^{48}\) A prolonged QTc or “long QT” indicates unusual electrical activity in the heart’s ventricles, as measured by an electrocardiogram (ECG). Symptoms can include fainting during stress or exercise, gasping while sleeping, deafness, muscle weakness, behavioral concerns, learning, memory, seizures, cardiac arrest, or sudden death (NIH, 2022).
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Evidence</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVIG</td>
<td>Inconclusive</td>
<td>Fever, headache, sore throat, nausea/vomiting, muscle/bone/joint pain, fatigue, irritability, anxiety, and aseptic meningitis.</td>
</tr>
<tr>
<td>Plasma exchange</td>
<td>Insufficient</td>
<td>Pallor, dizziness, nausea/vomiting, anxiety, reduction in serum calcium or potassium, paresthesias muscle spasms, arrhythmias, and anaphylaxis.</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Insufficient</td>
<td>Fever, headache, rash, fatigue, infection, hemolysis or other hemolytic reactions, anaphylaxis, renal failure, thrombosis, dermatological reactions, neutropenia, lung injury, seizures, and death.</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>Insufficient</td>
<td>Sensory disturbances, cytopenia, dizziness, nausea, diarrhea, abdominal pain, dermatologic reactions, hemolytic reactions, abnormal renal or hepatic function, malignant neoplasms, increased risk of sepsis or other infections, including cytomegalovirus, herpes zoster, BK virus, hepatitis B, and hepatitis C.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Insufficient</td>
<td>Insufficient evidence.</td>
</tr>
</tbody>
</table>


Key: CBT = cognitive behavioral therapy; C. diff = Clostridium difficile; IVIG = intravenous immunoglobulin; NSAIDs = nonsteroidal anti-inflammatory drugs.
BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the Policy Context section, AB 907, as amended on March 16, 2023, would require health plans regulated by the Department of Managed Health Care (DMHC) and health policies regulated by the California Department of Insurance (CDI) to provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). Covered treatments must include antibiotics, medications and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin (IVIG) therapy.

AB 907 applies to enrollees in health plans and health policies regulated by the Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI) as well as to beneficiaries in Medi-Cal. This section reports the potential incremental impacts of AB 907 on estimated baseline benefit coverage, utilization, and overall cost.

Analytic Approach and Key Assumptions

Assumptions regarding utilization

- To estimate utilization of diagnostic tests for PANDAS/PANS, CHBRP relied on published clinical guidelines to identify relevant diagnostic tests and estimate their frequency of use in diagnosis (Chang et al., 2015; Cooperstock et al., 2017; Frankovich et al., 2017; Pfeiffer et al., 2021; Thienemann et al., 2017). For more details on estimated utilization of diagnostic tests, see Appendix C, Tables 8 and 9.

- To estimate utilization of treatments for PANDAS/PANS, CHBRP used estimates from the literature (Frankovich et al., 2017; Thienemann et al., 2017), treatment guidelines from the PANDAS Physicians Treatment Network (Chang et al., 2015; Cooperstock et al., 2017; Frankovich et al., 2017; Pfeiffer et al., 2021; Thienemann et al., 2017), and consultations with a clinical expert. CHBRP assumed different treatment trajectories based on the severity of symptoms. For more details on estimated utilization of treatments for PANDAS/PANS, see Appendix C, Tables 8 and 9.

- At baseline and postmandate, a variety of access and supply barriers limit treatment utilization for PANDAS/PANS at baseline. These include:
  - There are few clinicians with knowledge of how to diagnose or treat PANDAS/PANS, and the few clinics currently accepting PANDAS/PANS patients accept only a small (<10%) of patients (Tang et al., 2021). Moreover, PANDAS/PANS treatment often requires multidisciplinary teams and coordination of care given the complexity of the syndromes and the myriad symptoms. Such multidisciplinary teams may be challenging to access for many families, and there are few clinics offering this type of multidisciplinary, specialized care (~10 in the United States). In California, there are only two clinics specializing in PANDAS/PANS care, one each at UCLA and Stanford, which may result in limited access. The lack of availability of clinics and physicians with knowledge and willingness to treat PANDAS/PANS often requires families to travel long distances to find care. A survey by O’Dor et al. (2022) of 441 primary caregivers of patients with PANDAS/PANS found that 16% of families reported traveling more than 500 miles for treatment and that 62% reported traveling more than 50 miles (O’Dor et al., 2022).

49 This includes approximately 73% of enrollees associated with the California Public Enrollees’ Retirement System (CalPERS).
Delayed diagnosis, misdiagnosis, and children’s suppression of behaviors during assessments are also treatment barriers in PANDAS/PANS identified in the literature (O’Dor et al., 2022; Tang et al., 2021).

As noted in the Background on PANDAS and PANS section, IVIG has been subject to intermittent national shortages due to growing demand as a treatment for various conditions and its manufacturing process (FDA, 2022; Rhodes, 2021).

As detailed in the Background on PANDAS and PANS and Medical Effectiveness sections, there is a lack of literature on effective treatments for PANDAS/PANS, which limits clinicians’ willingness to use various therapies such as plasma exchange and IVIG.

CHBRP assumed that the aforementioned diagnostic, access, and supply barriers would continue postmandate, resulting in low utilization of IVIG and plasma exchange.

- Access barriers are likely particularly acute among Medi-Cal enrollees, given low reimbursement rates and limited participation of providers and specialists. Moreover, other access barriers, such as transportation barriers and lower levels of health literacy with which to navigate a complex system may also limit Medi-Cal enrollees’ access to PANDAS/PANS care.

Assumptions regarding factors that would not change postmandate

- CHBRP assumed that carriers would still impose some utilization management strategies which would result in low rates of some PANDAS/PANS treatments utilization postmandate, specifically IVIG, plasma exchange, and rituximab.

- As detailed in the Policy Context section, CHBRP assumed that cost sharing for treatments outlined in the bill would not change.

- For some enrollees, medications are covered by and/or regulated by separate entities. Because AB 907 does not require creation of a pharmacy benefit – only compliant benefit coverage when a pharmacy benefit is present – baseline benefit coverage for enrollees without a pharmacy benefit or whose pharmacy benefit is not regulated by DMHC or CDI is compliant. See Table 2 in the Policy Context sections for assumptions about the coverage of pharmacy/medical benefits.

Additional assumptions

- CHBRP did not model the use of prophylactic antibiotic therapy or mycophenolate mofetil for PANDAS/PANS at baseline or postmandate given the lack of conclusive evidence on this practice and based on informal consultations with clinical experts in the field (Cooperstock et al., 2017; Pfeiffer et al., 2021).

For further details on the underlying data sources and methods used in this analysis, please see Appendix C.

Baseline and Postmandate Benefit Coverage

CHBRP queried health plans and policies in California to determine baseline benefit coverage and the impacts of AB 907.
Diagnostics for PANDAS/PANS

At baseline, 100% of enrollees with health insurance that would be subject to AB 907 have coverage that includes diagnostic tests associated with PANDAS/PANS recommended by various guidelines for diagnosing PANDAS/PANS. These include blood tests, throat cultures, and nose swabs. See Table 8 in Appendix C for a list of relevant diagnostic tests.

Treatment for PANDAS/PANS

At baseline, 100% of enrollees with health insurance that would be subject to AB 907 have coverage that includes some, but not all, treatments for PANDAS/PANS. Coverage by type of treatment varies substantially. CHBRP found that 100% of enrollees have health insurance that includes antibiotics commonly used for PANDAS/PANS and some oral prescription immunomodulatory medications including steroids and nonsteroidal anti-inflammatory medications (NSAIDs). Similarly, 100% of enrollees have health insurance that includes coverage for psychotropics used for treatment of neuropsychiatric symptoms of PANDAS/PANS, including selective serotonin receptor inhibitors (SSRIs), benzodiazepines, and antipsychotics. One hundred percent of enrollees also have health insurance that includes coverage of behavioral health therapies used for treatment of neuropsychiatric symptoms of PANDAS/PANS, including cognitive behavioral therapy (CBT).

Health plans and insurers generally use clinical guidelines to make medical necessity determinations about treatments such as IVIG, rituximab, and plasma exchange services, with some health plan/insurer policies for PANDAS/PANS noting that IVIG is not deemed medically necessary. Based on these policies, CHBRP estimates that 0% of enrollees have health insurance that includes coverage of IVIG, rituximab, and plasma exchange services for the treatment of PANDAS/PANS. Benefit coverage for relevant PANDAS/PANS services, including IVIG, rituximab, and plasma exchange services, among enrollees in commercial and CalPERS DMHC-regulated plans or CDI-regulated policies would increase to 100% based on the CHBRP assumption that all noncompliant plans and policies at baseline would become compliant postmandate.

Baseline and Postmandate Utilization

Diagnostics for PANDAS/PANS

CHBRP estimates that at baseline, 15,410 enrollees use diagnostic tests for PANDAS/PANS. These include various blood tests, throat cultures, and nose swabs. CHBRP estimates that for every 23 children tested for PANDAS/PANS using these diagnostic tests, 1 child is diagnosed with PANDAS/PANS and 22 children are not given this diagnosis. Given that 100% of enrollees already have baseline coverage, CHBRP estimates no changes in utilization for these diagnostic tests.

Treatment for PANDAS/PANS

At baseline, CHBRP estimates that 670 enrollees have a PANDAS/PANS diagnosis (Table 1). Among these enrollees, average annual utilization of oral prescription medications used for the treatment and management of neuropsychiatric symptoms (including medications such as antibiotics, steroids, NSAIDs, and psychotropics) is 17.8 prescriptions, each with a 30-day supply. At baseline, annual utilization of CBT is 20 visits per year. Given that 100% of enrollees already have baseline coverage, CHBRP estimates no changes in utilization for these diagnostic tests.

50 CHBRP estimated the number of enrollees who would use diagnostic tests for PANDAS/PANS by estimating the number of enrollees diagnosed annually with severe OCD. See Appendix C, Detailed Cost Notes Regarding Analysis-Specific Caveats and Assumptions for more detail about this assumption.

51 Refer to Appendix C for an explanation of how the prevalence of PANDAS/PANS was estimated.

52 See Appendix C Tables 8 and 9 for further explanation of how this baseline utilization was calculated.
medications and behavioral health therapies such as CBT, CHBRP estimated no changes in utilization of these specific medications and CBT services postmandate. See estimates in Table 1.

CHBRP estimates that IVIG, rituximab, and plasma exchange have extremely limited use at baseline. Although coverage of these therapies would increase to 100% postmandate, it is important to note that benefit coverage does not equate to utilization. As noted in the Analytic Approach and Key Assumptions section above, a variety of barriers limit access to such treatments at baseline and postmandate. These include a very limited number of providers with knowledge of how to treat PANDAS/PANS, a limited availability of clinics that offer such treatments, and supply shortages of these treatments. Moreover, continued use of utilization management approaches such as prior authorization may continue to limit access to IVIG, rituximab, and plasma exchange. CHBRP assumed that only enrollees with moderate or severe PANDAS/PANS would thus be prescribed and administered IVIG and rituximab. CHBRP assumed that within this group, only a small proportion (20%) of enrollees would be able to access these treatments postmandate due to the aforementioned supply and access barriers. Thus, CHBRP estimates that average annual utilization of IVIG among all enrollees with PANDAS/PANS would increase to 0.7 infusion therapy sessions per year. This results in an estimated 90 enrollees with moderate or severe PANDAS/PANS utilizing IVIG at least once per year, with greater expected utilization among those with severe PANDAS/PANS. CHBRP estimates that average annual utilization of rituximab would increase to 0.1 infusion therapy sessions. This results in an estimated 22 enrollees with severe PANDAS/PANS utilizing an average of 3 rituximab infusions per year. CHBRP estimated no change in the use of plasma exchange services given their low availability and the lack of evidence of their effectiveness in PANDAS/PANS.

Baseline and Postmandate Per-Unit Cost

Diagnostics for PANDAS/PANS

At baseline, CHBRP estimates that average per-unit costs of diagnostic tests are $30. The estimated average cost per enrollee is $270. CHBRP estimates no impact on unit cost would be expected postmandate.

Treatment for PANDAS/PANS

At baseline, CHBRP estimates that average per-prescription costs of oral prescription medications, including antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs, selective serotonin uptake inhibitors, benzodiazepines, and antipsychotics, is $7 for a 30-day supply, the per-visit cost of CBT is $142, the per-unit cost of a rituximab infusion session is $9,566, the per-unit cost of IVIG is $4,312, and the per-unit cost of a plasma exchange therapy session is $2,136. CHBRP estimates no impact on unit cost postmandate for any of these therapies.

Baseline and Postmandate Expenditures

Table 4 and Table 5 present baseline and postmandate expenditures by market segment for DMHC-regulated plans and CDI-regulated policies. The tables present per member per month (PMPM) premiums, enrollee expenses for both covered and noncovered benefits, and total expenditures (premiums as well as enrollee expenses).

AB 907 would increase total net annual expenditures by total net annual $2,990,000, or total net annual 0.0020%, for enrollees with DMHC-regulated plans (including DMHC-regulated Medi-Cal Managed Care

53 This estimate is based on informal consultations with clinical experts in PANDAS/PANS.
54 Cost estimates are estimated using both commercial and Medi-Cal claims data. See Appendix C for more details.
Plans) and CDI-regulated policies. This is due to a $2,838,000 increase in total health insurance premiums, plus $153,000 paid by enrollees for covered and/or noncovered benefits.

**Premiums**

Overall, CHBRP estimates premiums would increase by $2,837,000 postmandate as a result of AB 907. Changes in premiums as a result of AB 907 would vary by market segment. Note that such changes are related to the number of enrollees (see Table 1, Table 4, and Table 5), with health insurance that would be subject to AB 907. The largest increases are among large group plans in DMHC-regulated plans ($0.0098 PMPM, a 0.0016% increase). The smallest increases are among DMHC-regulated individual plans ($0.0034 PMPM, a 0.0005% increase), DMHC-regulated Medi-Cal 65+ plans (no change), and CDI-regulated individual plans ($0.0044 PMPM, a 0.0007% increase).

For Medi-Cal beneficiaries enrolled in DMHC-regulated plans, among those under 65, premiums would increase by $0.0152 (a 0.0060% increase), and among those 65 and over, there would be no impact. In addition to the estimated $1,471,000 increase in premiums for the 8.8 million Medi-Cal beneficiaries enrolled in DMHC-regulated plans, a proportional increase of $370,000 is estimated to occur for the 2.0 million beneficiaries enrolled in county organized health system (COHS) managed care. CHBRP assumes the two populations to be relatively similar and to have relatively similar benefit coverage.

**Enrollee Expenses**

AB 907-related changes in cost sharing for covered benefits (deductibles, copays, etc.) and out-of-pocket expenses for noncovered benefits would vary by market segment. Note that such changes are related to the number of enrollees (see Table 1, Table 4, and Table 5) with health insurance that would be subject to AB 907 expected to use the relevant treatments during the year after enactment.

CHBRP projects no change to copayments or coinsurance rates but does project an increase in utilization of two treatments for PANDAS/PANS – IVIG and rituximab – and therefore an increase in enrollee cost sharing. It is possible that some enrollees incurred expenses related to IVIG, rituximab infusions, or plasma exchange therapy at baseline for which coverage was denied, but CHBRP cannot estimate the frequency with which such situations occur and so cannot offer a calculation of impact.

CHBRP finds the largest increases in enrollee cost sharing for covered benefits are for enrollees in individual plans and small group plans (see Table 5). Increases in enrollee cost sharing in individual plans range from $0.0009 PMPM in DMHC-regulated plans to $0.0014 PMPM in CDI-regulated plans. Increases in enrollee cost sharing in small group plans range from $0.0016 PMPM in DMHC-regulated plans to $0.0020 PMPM in CDI-regulated plans.

**Potential Cost Offsets of Savings in the First 12 Months After Enactment**

CHBRP does not project any cost offsets or savings in health care that would result because of the enactment of provisions in AB 907. While it is possible that use of treatments and services for PANDAS/PANS such as early use of IVIG or rituximab could reduce psychiatric-related hospitalizations, CHBRP is unable to quantify the fiscal impacts of these changes due to lack of conclusive evidence about the effectiveness of these treatments.

**Postmandate Administrative Expenses and Other Expenses**

CHBRP estimates that the increase in administrative costs of DMHC-regulated plans and/or CDI-regulated policies will remain proportional to the increase in premiums. CHBRP assumes that if health care costs increase as a result of increased utilization or changes in unit costs, there is a corresponding proportional increase in administrative costs. CHBRP assumes that the administrative cost portion of premiums is unchanged. All health plans and insurers include a component for administration and profit in their premiums.
Other Considerations for Policymakers

In addition to the impacts a bill may have on benefit coverage, utilization, and cost, related considerations for policymakers are discussed below.

Postmandate Changes in the Number of Uninsured Persons

Because the change in average premiums does not exceed 1% for any market segment (see Table 1, Table 4, and Table 5), CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of AB 907.

Changes in Public Program Enrollment

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs due to the enactment of AB 907.

How Lack of Benefit Coverage Results in Cost Shifts to Other Payers

Certain treatments for PANDAS/PANS (e.g., IVIG, rituximab, plasma exchange) are generally self-funded when there is no coverage and there may be some opportunity for enrollees without coverage to seek help via grant or loan programs through private organizations. A small number of Medi-Cal enrollees may be able to obtain assistance from California’s Children’s Services (CCS), but CHBRP is unable to estimate the exact number due to the medical review criteria necessary for CCS eligibility. In California, unreimbursed medical expenses are income tax deductible, following the federal deductibility threshold. CHBRP is unable to provide a quantifiable estimate of shifts from private grant and loan funding to health plans and programs postmandate.
Table 4. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2024

<table>
<thead>
<tr>
<th></th>
<th>DMHC-Regulated</th>
<th>Publicly Funded Plans</th>
<th>CDI-Regulated</th>
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<tbody>
<tr>
<td></td>
<td>Commercial Plans (by Market) (a)</td>
<td>Medi-Cal (Excludes COHS) (c)</td>
<td>Commercial Plans (by Market) (a)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large Group</td>
<td>Small Group</td>
<td>Individual</td>
<td>CalPER S (b)</td>
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<tr>
<td>Enrollee counts</td>
<td></td>
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<td></td>
<td>371,000</td>
</tr>
<tr>
<td>Total enrollees in</td>
<td>7,780,000</td>
<td>2,212,000</td>
<td>2,618,000</td>
<td>882,000</td>
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<tr>
<td>plans/policies</td>
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<td>371,000</td>
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<tr>
<td>subject to state</td>
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<td>371,000</td>
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<tr>
<td>mandates (d)</td>
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<td>Total enrollees in</td>
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</tr>
<tr>
<td>(deductibles, copays,</td>
<td></td>
<td></td>
<td></td>
<td>$99.22</td>
</tr>
<tr>
<td>etc.)</td>
<td>$40.98</td>
<td>$127.06</td>
<td>$168.73</td>
<td>$49.17</td>
</tr>
<tr>
<td>Expenses for</td>
<td></td>
<td></td>
<td></td>
<td>$0.00</td>
</tr>
<tr>
<td>noncovered benefits (f)</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
</tr>
<tr>
<td>Total expenditures</td>
<td>$636.33</td>
<td>$724.29</td>
<td>$814.06</td>
<td>$744.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$770.40</td>
</tr>
</tbody>
</table>


Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state’s health insurance marketplace).
(b) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.1% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC. CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. Includes those who are also Medicare beneficiaries.

(d) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California, CalPERS, or Medi-Cal.

(e) In some cases, a union or other organization – or Medi-Cal for its beneficiaries.

(f) Includes only those expenses that are paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS = California Public Employees’ Retirement System; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care.


Table 5. Postmandate Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2024

<table>
<thead>
<tr>
<th>DMHC-Regulated</th>
<th>CDI-Regulated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Commercial Plans (by Market) (a)</td>
</tr>
<tr>
<td></td>
<td>Large Group</td>
</tr>
<tr>
<td>Enrollee counts</td>
<td>7,780,000</td>
</tr>
<tr>
<td>Total enrollees in plans/policies subject to state mandates (d)</td>
<td></td>
</tr>
<tr>
<td>Total enrollees in plans/policies subject to AB 907</td>
<td>7,780,000</td>
</tr>
<tr>
<td>Premium costs</td>
<td></td>
</tr>
<tr>
<td>Average portion of premium paid by employer (e)</td>
<td>$0.0078</td>
</tr>
<tr>
<td>Average portion of premium paid by enrollee</td>
<td>$0.0020</td>
</tr>
<tr>
<td>Total premium</td>
<td>$0.0098</td>
</tr>
<tr>
<td>Enrollee expenses</td>
<td></td>
</tr>
<tr>
<td>Cost sharing for covered benefits (deductibles, copays, etc.)</td>
<td>$0.0007</td>
</tr>
<tr>
<td>Expenses for noncovered benefits (f)</td>
<td>$0.0000</td>
</tr>
<tr>
<td>Total expenditures</td>
<td>$0.0105</td>
</tr>
<tr>
<td>Postmandate percent change</td>
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</tr>
<tr>
<td>Percent change insured premiums</td>
<td>0.0016%</td>
</tr>
<tr>
<td>Percent change total expenditures</td>
<td>0.0016%</td>
</tr>
</tbody>
</table>


Notes: (a) Includes enrollees with grandfathered and non-grandfathered health insurance acquired outside or through Covered California (the state’s health insurance marketplace).
(b) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.71% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC. CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. Includes those who are also Medicare beneficiaries.

(d) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California, CalPERS, or Medi-Cal.

(e) In some cases, a union or other organization – or Medi-Cal for its beneficiaries.

(f) Includes only those expenses that are paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS = California Public Employees' Retirement System; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care.

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58 For more detail, see CHBRP’s resource, Sources of Health Insurance in California, available at http://chbrp.org/other_publications/index.php.
PUBLIC HEALTH IMPACTS

As discussed in the Policy Context section, AB 907 would mandate coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). Covered treatments must include antibiotics, medication and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin therapy).

The public health impact analysis includes estimated impacts in the short term (within 12 months of implementation) and in the long term (beyond the first 12 months postmandate). This section estimates the short-term impact59 of AB 907 on the reduction of symptoms associated with PANDAS/PANS, potential treatment harms, and financial burden.

Estimated Public Health Outcomes

As presented in Medical Effectiveness, evidence of effective treatments for PANDAS/PANS is lacking. Of 10 treatments evaluated by CHBRP, evidence of effectiveness for 2 treatment types was inconclusive due to conflicting findings among few studies with small sample sizes. The remaining 8 treatment types had insufficient evidence to assess their effectiveness in mitigating or eliminating symptoms of these syndromes.

As presented in the Benefit Coverage, Utilization, and Cost Impacts section, CHBRP estimates that 670 children with insurance subject to AB 907 would have a diagnosis of PANDAS/PANS. Based on responses from health plans and insurers, baseline coverage for the diagnosis and treatment of PANDAS/PANS is 100% with the exception of intravenous immunoglobulin (IVIG), rituximab and plasma exchange, which may be prescribed for moderate to severe cases. In the first 12 months postmandate, CHBRP projects an increase of 67 doses of rituximab and 469 sessions of IVIG for the enrollees with moderate and severe cases of PANDAS/PANS (about 442 enrollees or two-thirds of those diagnosed). See Appendix C for calculations.

Based on the evidence, PANDAS/PANS are rare syndromes, not well-recognized, and subject to controversy. In the first 12 months postmandate, CHBRP is unable to project a health impact associated with AB 907 due to the lack of evidence of treatment effectiveness. On an individual basis, enrollees with severe cases who use IVIG, rituximab, or plasma exchange due to new coverage, may see a reduction or elimination of symptoms on a case-by-case basis. However, these enrollees may still experience barriers to accessing IVIG, rituximab, and plasma exchange due to national shortages and/or potential insurance utilization management requirements. There is insufficient evidence to ascertain whether the potential harms from these two treatments and plasma exchange outweigh the potential treatment benefits. Due to the lack of research, CHBRP is unable to include a discussion of disparities among PANDAS/PANS patients.

In the first year postmandate, the public health impact of AB 907 for the newly covered 670 children with PANDAS/PANS is unknown due to insufficient and inconclusive evidence regarding the effectiveness of treatments for PANDAS/PANS. Please note that the absence of evidence is not “evidence of no effect.” It is possible that an impact – desirable or undesirable – could result, but current evidence is insufficient to inform an estimate.

Enrollee Financial Burden

Rituximab, IVIG, and plasma exchange are the treatments that would be newly covered under AB 907 with estimated costs of $9,600, $4,300, and $2,100 per session, respectively (see Table 1). CHBRP

59 CHBRP defines short-term impacts as changes occurring within 12 months of bill implementation.
assumes some families paid for these treatments out-of-pocket. However, due to a lack of information about the type and number of treatment sessions paid for at baseline and unknown effects of utilization management postmandate, CHBRP is unable to project the impact of AB 907 on out-of-pocket expenses for previously uncovered treatments.
LONG-TERM IMPACTS

In this section, CHBRP estimates the long-term impact of AB 907 which CHBRP defines as impacts occurring beyond the first 12 months after implementation. These estimates are qualitative and based on the existing evidence available in the literature. CHBRP does not provide quantitative estimates of long-term impacts because of unknown improvements in clinical care, changes in prices, implementation of other complementary or conflicting policies, and other unexpected factors.

Long-Term Utilization and Cost Impacts

Utilization Impacts

Utilization of diagnostic tests and treatments for PANDAS/PANS is expected to be similar in the long term as utilization in the first 12 months postmandate. However, should evidence about the effectiveness of new diagnostic tests or treatments such as IVIG or rituximab become more conclusive, for example, via more evidence from larger randomized controlled clinical trials, more physicians may prescribe these treatments.

Cost Impacts

Cost impacts are expected to also be similar to those projected in the first 12 months postmandate.

Long-Term Public Health Impacts

Some interventions in proposed mandates provide immediate measurable impacts (e.g., maternity service coverage or acute care treatments), whereas other interventions may take years to make a measurable impact (e.g., coverage for tobacco cessation or vaccinations). When possible, CHBRP estimates the long-term effects (beyond 12 months postmandate) to the public’s health that would be attributable to the mandate, including impacts disparities, premature death, and economic loss.

Due to the dearth of research about PANDAS/PANS, CHBRP finds an unknown health impact of AB 907 over the long term.

It is possible that growing awareness of PANDAS and PANS statewide may increase the number of children diagnosed and treated, with an unknown, but potentially beneficial effect on child and family quality of life and school performance.
APPENDIX A TEXT OF BILL ANALYZED

The California Assembly Committee on Health requested that CHBRP analyze AB 907, as amended on March 16, 2023.

AMENDED IN ASSEMBLY MARCH 16, 2023

CALIFORNIA LEGISLATURE—2023–2024 REGULAR SESSION

ASSEMBLY BILL NO. 907

Introduced by Assembly Member Lowenthal

February 14, 2023

An act to add Section 1367.38 to the Health and Safety Code, and to add Section 10123.38 to the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL’S DIGEST

AB 907, as amended, Lowenthal. Coverage for PANDAS and PANS.

Existing law, the Knox-Keene Health Care Service Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care, and makes a willful violation of the act a crime. Existing law provides for the regulation of health insurers by the Department of Insurance. Existing law sets forth specified coverage requirements for health care service plan contracts and health insurance policies, and limits the copayment, coinsurance, deductible, and other cost sharing that may be imposed for specified health care services.

This bill would require a health care service plan contract or health insurance policy issued, amended, or renewed on or after January 1, 2024, to provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) that is prescribed or ordered by a provider. The bill would prohibit coverage for PANDAS and PANS from being subject to a copayment, coinsurance, deductible, or other cost sharing that is greater than that applied to other similar benefits. The bill would prohibit a plan or insurer from denying or delaying coverage for medically necessary treatment of PANDAS or PANS solely because the enrollee or insured previously received treatment for the condition under a different diagnostic name. Because a willful violation of these provisions by a health care service plan would be a crime, the bill would impose a state-mandated local program.
The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority    Appropriation: no    Fiscal Committee: yes    Local Program: yes

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. Section 1367.38 is added to the Health and Safety Code, to read:

1367.38. (a) A health care service plan contract issued, amended, or renewed on or after January 1, 2024, shall provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) that is prescribed or ordered by a provider. Treatment for PANDAS and PANS that shall be covered includes antibiotics, medication and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin therapy.

(b) Coverage for PANDAS and PANS shall not be subject to a copayment, coinsurance, deductible, or other cost sharing that is greater than that applied to other similar benefits provided by the contract.

(c) (1) Coverage Any required authorization for PANDAS and PANS prophylaxis, diagnosis, or treatment shall be provided in a timely manner that is appropriate for the severity of an enrollee’s condition pursuant to Section 1367.03.

(2) A health care service plan shall not deny or delay coverage for medically necessary treatment of PANDAS or PANS solely because the enrollee previously received treatment, including the same or similar treatment, for PANDAS or PANS, or because the enrollee has been diagnosed with or received treatment for their condition under a different diagnostic name, including autoimmune encephalopathy.

(3) Coverage for any form of medically necessary treatment shall not be limited over a lifetime of an enrollee or by contract period.

(4) This section does not prohibit a plan from requesting treatment notes and anticipated duration of treatment and outcomes from a provider.

(3) A health care service plan shall not limit coverage of immunomodulating therapies for PANDAS or PANS in a manner that is inconsistent with the treatment recommendations pursuant to subdivision (d), and shall not require a trial of therapies that treat only neuropsychiatric symptoms before authorizing coverage of immunomodulating therapies pursuant to this section.
(d) Coverage for PANDAS and PANS shall adhere to the treatment recommendations developed by a consortium of medical professionals convened to research, identify, and publish best practice clinical practice guidelines and evidence-based standards for the diagnosis and treatment of those disorders that are accessible to providers and are based on evidence of positive patient outcomes.

(e) For billing and diagnostic purposes, PANDAS and PANS shall be coded as autoimmune encephalitis until the American Medical Association and the federal Centers for Medicare and Medicaid Services create and assign a specific code or codes for PANDAS and PANS. After the creation of that code or codes, PANDAS and PANS may be coded as autoimmune encephalitis, PANDAS, or PANS. If PANDAS or PANS is known by a different common name in the future, it may be coded under that name and this section shall apply to that disorder or syndrome.

(f) This section does not apply to a specialized health care service plan contract that does not cover an essential health benefit, as defined in Section 1367.005, or a Medicare supplement policy.

SEC. 2. Section 10123.38 is added to the Insurance Code, to read:

10123.38. (a) A health insurance policy issued, amended, or renewed on or after January 1, 2024, shall provide coverage for the prophylaxis, diagnosis, and treatment of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) that is prescribed or ordered by a provider. Treatment for PANDAS and PANS that shall be covered includes antibiotics, medication and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and intravenous immunoglobulin therapy.

(b) Coverage for PANDAS and PANS shall not be subject to a copayment, coinsurance, deductible, or other cost sharing that is greater than that applied to other similar benefits provided by the policy.

(c) (1) Coverage. Any required authorization for PANDAS and PANS prophylaxis, diagnosis, or treatment shall be provided in a timely manner that is appropriate for the severity of an insured’s condition pursuant to Section 10133.54.

(2) A health insurer shall not deny or delay coverage for medically necessary treatment of PANDAS or PANS solely therapies because the insured previously received treatment, including the same or similar treatment, for PANDAS or PANS, or because the insured has been diagnosed with or received treatment for their condition under a different diagnostic name, including autoimmune encephalopathy.

(3) Coverage for any form of medically necessary treatment shall not be limited over a lifetime of an insured or by policy period.

(4) This section does not prohibit an insurer from requesting treatment notes and anticipated duration of treatment and outcomes from a provider.
(3) A health insurer shall not limit coverage of immunomodulating therapies for PANDAS or PANS in a manner that is inconsistent with the treatment recommendations pursuant to subdivision (d), and shall not require a trial of therapies that treat only neuropsychiatric symptoms before authorizing coverage of immunomodulating therapies pursuant to this section.

(d) Coverage for PANDAS and PANS shall adhere to the treatment recommendations developed by a consortium of medical professionals convened to research, identify, and publish best practice clinical practice guidelines and evidence-based standards for the diagnosis and treatment of those disorders that are accessible to providers and are based on evidence of positive patient outcomes. Disorders.

(e) For billing and diagnostic purposes, PANDAS and PANS shall be coded as autoimmune encephalitis until the American Medical Association and the federal Centers for Medicare and Medicaid Services create and assign a specific code or codes for PANDAS and PANS. After the creation of that code or codes, PANDAS and PANS may be coded as autoimmune encephalitis, PANDAS, or PANS. If PANDAS or PANS is known by a different common name in the future, it may be coded under that name and this section shall apply to that disorder or syndrome.

(f) This section does not apply to a specialized health insurance policy that does not cover an essential health benefit, as defined in Section 10112.27, or a Medicare supplement policy.

SEC. 3. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.
APPENDIX B LITERATURE REVIEW METHODS

This appendix describes methods used in the literature review conducted for this report. A discussion of CHBRP’s system for medical effectiveness grading evidence follows.

Studies of the effects of antibiotics, psychotropics, behavioral therapy, plasma exchange, intravenous immunoglobulin (IVIG) therapy and other immunomodulating medications were identified through searches of PubMed, CINAHL Complete, PsycInfo, Scopus, Web of Science Core Collection, EconLit, Business Source Complete. The search was limited to abstracts of studies published in English, persons diagnosed with Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) and/or Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS). The search was limited to studies published from 2017 to present, CHBRP relied on a systematic review published in 2018 for findings from studies published prior to 2017.

Reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria.

Medical Effectiveness Review

The medical effectiveness literature review returned abstracts for 129 articles, of which 14 were reviewed for inclusion in this report. A total of 11 studies were included in the medical effectiveness review for AB 907.

Medical Effectiveness Evidence Grading System

In making a “call” for each outcome measure, the medical effectiveness lead and the content expert consider the number of studies as well the strength of the evidence. Further information about the criteria CHBRP uses to evaluate evidence of medical effectiveness can be found in CHBRP’s Medical Effectiveness Analysis Research Approach. To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design;
- Statistical significance;
- Direction of effect;
- Size of effect; and
- Generalizability of findings.

The grading system also contains an overall conclusion that encompasses findings in these five domains. The conclusion is a statement that captures the strength and consistency of the evidence of an intervention’s effect on an outcome. The following terms are used to characterize the body of evidence regarding an outcome:

- Clear and convincing evidence;
- Preponderance of evidence;
- Limited evidence;
- Inconclusive evidence; and
- Insufficient evidence.

60 Available at: www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.
A grade of *clear and convincing evidence* indicates that there are multiple studies of a treatment and that the *large majority* of studies are of high quality and consistently find that the treatment is either effective or not effective.

A grade of *preponderance of evidence* indicates that the *majority* of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

A grade of *limited evidence* indicates that the studies had limited generalizability to the population of interest and/or the studies had a fatal flaw in research design or implementation.

A grade of *inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

A grade of *insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.
Appendix C  Cost Impact Analysis: Data Sources, Caveats, and Assumptions

With the assistance of CHBRP’s contracted actuarial firm, Milliman, Inc, the cost analysis presented in this report was prepared by the faculty and researchers connected to CHBRP’s Task Force with expertise in health economics. Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP’s cost impacts analyses are available at CHBRP’s website.

This appendix describes analysis-specific data sources, estimation methods, caveats, and assumptions used in preparing this cost impact analysis.

Analysis-Specific Data Sources

Current coverage of tests, treatments, and services for commercial enrollees was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent 82% of commercial enrollees with health insurance that can be subject to state benefit mandates. In addition, CalPERS, DHCS, and the four largest (by enrollment) DMHC-regulated plans enrolling Medi-Cal beneficiaries were queried regarding related benefit coverage. As necessary, CHBRP extrapolated from responses of similarly situated plans/policies.

For this analysis, CHBRP relied on CPT codes to identify relevant services. CPT copyright 2023 American Medical Association. All rights reserved. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. CPT is a registered trademark of the American Medical Association.

Detailed Cost Notes Regarding Analysis-Specific Caveats and Assumptions

The analytic approach and key assumptions are determined by the subject matter and language of the bill being analyzed. As a result, analytic approaches may differ between topically similar analyses, and therefore the approach and findings may not be directly comparable.

- CHBRP used Milliman’s 2021 Consolidated Health Cost Guidelines Sources Database (CHSD) to estimate annual average cost for PANDAS/PANS diagnostic tests and treatments in 2024. CHBRP calculated the baseline average cost for PANDAS/PANS diagnostic tests, prescription medications, and services such as IVIG, plasma exchange, and rituximab per unit by dividing the total allowed dollars observed in the data for the selected treatments and services by the total units observed in the data for the selected treatments and services. CHBRP assumed an annual increase in costs over time between 2.85% and 4.50%, depending on the type of service.

- Estimated annual average cost for PANDAS/PANS diagnostic tests and treatments in 2024 were calculated using an average of commercial and Medi-Cal claims data.

- Based on the literature and consultations with a clinical expert, CHBRP assumed that new onset cases of PANDAS/PANS primarily occur in children 17 years of age and younger.

- The prevalence of PANDAS/PANS has not been well described in the literature. CHBRP estimated the prevalence of PANDAS/PANS using a combination of estimates from the literature and consultation with a clinical experts. CHBRP assumed a prevalence of PANDAS/PANS of

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61 CHBRP’s authorizing statute, available at https://chbrp.org/about_chbrp/index.php, requires that CHBRP use a certified actuary or “other person with relevant knowledge and expertise” to determine financial impact.

62 See method documents posted at www.chbrp.org/about/analysis-methodology/cost-impact-analysis; in particular, see Cost Analyses: Data Sources, Caveats, and Assumptions.
1/10,000 (Kronenberg and Shouldice, 2019). Using this prevalence, and estimating that about 6.7 million enrollees 17 years of age and younger are subject to the benefit mandate, CHBRP estimated that 670 children 17 years of age and younger are diagnosed with PANDAS/PANS annually.

- To estimate the diagnostic test utilization, CHBRP assumed a 1-year incidence of onset OCD of 0.7% (Valleni-Basile et al., 1996). CHBRP assumed that of these new-onset cases, 33% had severe OCD, for which tests for PANDAS/PANS would be recommended (Gilbert et al., 2018). CHBRP estimated the number of children 12 years of age and younger with utilization of diagnostic tests for PANDAS/PANS by multiplying the total number of enrollees ages 12 and younger subject to the benefit mandate by the 1-year incidence of onset OCD (0.7%) and then multiplying this number by 0.333.

- CHBRP reviewed CHSD data for patients diagnosed with PANDAS/PANS using logic outlined in Table 6. CHBRP estimated utilization amounts for three different severity levels (mild, moderate, severe) based on discussions with content experts and a review of literature.

**Table 6. ICD-10 Codes Used to Identify PANDAS/PANS Service Utilization**

<table>
<thead>
<tr>
<th>Condition</th>
<th>How Identified</th>
</tr>
</thead>
</table>
| PANDAS    | Must include ICD-10 code: D89.89.  
            Then also include one of the following: OCD, tic disorder, panic disorder, depression, eating disorders |
| PANS      | ICD-10 code: G04.81 (for autoimmune encephalitis)  
            Then also include one of the following: OCD, tic disorder, panic disorder, depression, eating disorders |
| OCD       | F42.2, F42.8, F42.9, F60.5 |
| Tic disorder | F95.0-F95.9 |
| Panic disorder | F41.0-F41.3, F41.8, F41.9 |
| Depression | F32.0-F32.5, F33.0-F33.5 |
| Eating disorders | F50.0-F50.9 |

*Source: California Health Benefits Review Program, 2023.*

- The following table shows the assumed distribution of PANDAS/PANS cases between mild, moderate, and severe. This assumption was made based on informal conversations with PANDAS/PANS clinical experts.

**Table 7. Distribution of PANDAS/PANS Severity**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>33.33%</td>
</tr>
<tr>
<td>Moderate</td>
<td>33.33%</td>
</tr>
<tr>
<td>Severe</td>
<td>33.33%</td>
</tr>
</tbody>
</table>

*Source: California Health Benefits Review Program, 2023; informal discussions with PANDAS/PANS clinical expert.*
Table 8 identifies all services included in the estimated treatment plans by severity level for PANDAS/PANS. The table shows the Table 1 category for each service/treatment, and the language included in the bill. Finally, it also shows how the service/treatment is identified, either with a national drug code (NDC) for prescription drugs, or by CPT codes. CHBRP only modeled diagnostics and treatments that are included in the PANDAS/PANS guidelines discussed earlier in the report. There is one exception – the prescription drug mycophenolate mofetil is in the guidelines but was excluded from the analysis based on the recommendations of clinical experts. Note that prescription drugs contain many NDCs. For simplicity, CHBRP chose one common generic drug NDC to use for each drug category. In practice, there are many suitable prescription drug options that could be prescribed from these drug categories.

In Table 9, the utilization numbers represent the assumed annual utilization per enrollee with PANDAS/PANS, with the following exceptions.

- The utilization for IVIG is assumed to be dampened by a factor of 0.2. This is due to a variety of issues that will limit the utilization of IVIG, as discussed more fully in the Benefit Coverage, Utilization, and Cost Impacts section.
- The utilization for all diagnostic tests is not per enrollee with PANDAS/PANS, but rather per enrollee that undergoes diagnostic testing to determine if the child has PANDAS/PANS. CHBRP estimated that for every PANDAS/PANS diagnosis, there are 22 children who are tested for it who do not receive a diagnosis for it.

For each Table 1 category, CHBRP took the average cost per procedure for all treatments and services aggregated within the category.

Table 8. Services Included in Estimated Treatment Plans by Severity Level

<table>
<thead>
<tr>
<th>Language in Bill</th>
<th>Services/Treatments</th>
<th>Table 1 Category</th>
<th>How Identified</th>
<th>Assumed Annual Utilization by Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Amoxicillin</td>
<td>Prescription</td>
<td>NDC: 65862001705</td>
<td>Mild: 1/2 month, Moderate: 1/2 month, Severe: 1/2 month</td>
</tr>
<tr>
<td>Immunomodulating medications</td>
<td>Corticosteroids</td>
<td>Prescription</td>
<td>NDC: 00054001825</td>
<td>Mild: 2 months, Moderate: 2 months, Severe: 2 months</td>
</tr>
<tr>
<td>Immunomodulating medications</td>
<td>Nonsteroidal anti-inflammatory</td>
<td>Prescription</td>
<td>NDC: 64380080707</td>
<td>Mild: 2 months, Moderate: 2 months, Severe: 2 months</td>
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<td>Medication therapies to</td>
<td>Selective serotonin uptake</td>
<td>Prescription</td>
<td>NDC: 50111064801</td>
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<td>manage neuropsychiatric</td>
<td>inhibitors</td>
<td>Prescription</td>
<td>NDC: 65862067799</td>
<td>Mild: None, Moderate: 2 months, Severe: 12 months</td>
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<tr>
<td>symptoms of PANS</td>
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<td>Medication therapies to</td>
<td>Benzodiazepines</td>
<td>Prescription</td>
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<td>manage neuropsychiatric</td>
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<td>symptoms of PANS</td>
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<td>Antipsychotics</td>
<td>Prescription</td>
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<td>Behavioral health</td>
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<td>CPT Codes: 90791,</td>
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<td>therapies to manage</td>
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<td>90832, 90834, 90837</td>
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<td>neuropsychiatric symptoms of</td>
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<td>PANS</td>
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<td>Plasma exchange</td>
<td>Plasma exchange</td>
<td>Plasma exchange</td>
<td>CPT Codes: 36514,</td>
<td>Mild: None, Moderate: None, Severe: None</td>
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<td>36516</td>
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<td>Intravenous immunoglobulin</td>
<td>Intravenous immunoglobulin</td>
<td>IVIG infusions</td>
<td>CPT Codes for</td>
<td>Mild: None, Moderate: 1 infusion, Severe: 9 infusions</td>
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<td>therapy</td>
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<td>administration: 96365,</td>
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<td>96366, 96368 J-Code for</td>
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<td>drug cost: J1459, J1554,</td>
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<td>J1556, J1557, J1561, J1566,</td>
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### Table 1 Category

<table>
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<tr>
<th>Coverage at Baseline</th>
<th>Coverage Postmandate</th>
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</thead>
</table>

- **Diagnostics**
  - Group A Beta-Hemolytic *Streptococcus* with throat culture
  - ASO (blood test)
  - AntiD-Nase-B
  - CBC with differential
  - Antinuclear with antibody titers
  - Quantitative immunoglobulins
  - *Mycoplasma pneumoniae*, DNA PCR
  - *Mycoplasma pneumoniae*, antibodies, IgG, IgM

- **Prescription medication**

- **Psychology visits**

- **Immunomodulating infusion therapy – IVIG session**

- **Immunomodulating infusion therapy - rituximab**

- **Plasma exchange session**

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*Source: California Health Benefits Review Program, 2023.*

Based on the average cost calculated from the CHSD data and the utilization estimated by the content expert, CHBRP developed average annual costs of all PANDAS/PANS diagnosis and treatment services, per PANDAS/PANS enrollee pre- and postmandate. CHBRP assumed that the services are subject to an average cost-sharing of 11.8% for all plans that are not Medi-Cal, and assumed no cost sharing for the Medi-Cal plans. CHBRP did not model self-pay for any of these services pre-mandate. The baseline and postmandate coverage assumptions were based on the carrier surveys, and are shown in the table below.

### Table 9. Coverage Assumptions of Treatments

<table>
<thead>
<tr>
<th>Coverage at Baseline</th>
<th>Coverage Postmandate</th>
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- **Diagnostics**
  - 100%

- **Prescription medication**
  - 100%

- **Psychology visits**
  - 100%

- **Immunomodulating infusion therapy – IVIG session**
  - 0%

- **Immunomodulating infusion therapy - rituximab**
  - 0%

- **Plasma exchange session**
  - 0%

*Source: California Health Benefits Review Program, 2023.*

Note that while CHBRP included the average cost of plasma exchange in Table 1, CHBRP does not expect the change in coverage for this service to result in any additional costs to the DMHC-regulated plan or CDI-regulated policy.
CHBRP did not include the use of MRI or EEG tests when considering diagnostic tests for PANDAS/PANS, as these are typically used to diagnose or rule out other conditions (PANDAS Physicians Network 2023).

**Determining Public Demand for the Proposed Mandate**

CHBRP reviews public demand for benefits by comparing the benefits provided by self-insured health plans or policies (which are not regulated by the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS have the largest number of enrollees. The CalPERS PPOs currently provide benefit coverage similar to what is available through group health insurance plans and policies that would be subject to the mandate.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask plans and insurers who act as third-party administrators for (non-CalPERS) self-insured group health insurance programs whether the relevant benefit coverage differed from what is offered in group market plans or policies that would be subject to the mandate. The responses indicated that there were no substantive differences.

**Second-Year Impacts on Benefit Coverage, Utilization, and Cost**

CHBRP has considered whether continued implementation during the second year of the benefit coverage requirements of AB 907 would have a substantially different impact on utilization of either the tests, treatments, or services for which coverage was directly addressed, the utilization of any indirectly affected utilization, or both. CHBRP reviewed the literature and consulted content experts about the possibility of varied second-year impacts and determined the second year’s impacts of AB 907 would be substantially the same as the impacts in the first year (see Table 1). Minor changes to utilization and expenditures are due to population changes between the first year postmandate and the second year postmandate.
REFERENCES


Kronenberg S, Shouldice M. Frequency and Impact of PANDAS/PANS Diagnosis. Ottawa, ON, Canada: Canadian Paediatric Surveillance Program; 2019.


CALIFORNIA HEALTH BENEFITS REVIEW PROGRAM
COMMITTEES AND STAFF

A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP Faculty Task Force comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are Task Force Contributors to CHBRP from UC that conduct much of the analysis. The CHBRP staff coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and manages all external communications, including those with the California Legislature. As required by CHBRP’s authorizing legislation, UC contracts with a certified actuary, Milliman, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit.

The National Advisory Council provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance of its National Advisory Council. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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Joy Melnikow, MD, MPH, Marykate Miller, MS, of the University of California, Davis, prepared the medical effectiveness analysis. Stephen L. Clancy, MLS, of the University of California, Irvine, conducted the literature search. Joy Melnikow, MD, MPH, Dominique Ritley, MPH, and Katrine Padilla, MPP, all of the University of California, Davis, prepared the public health impact analysis. Michelle Keller, PhD, MPH, of the University of California, Los Angeles, prepared the cost impact analysis. Matt Schoonmaker, FSA, MAAA, provided actuarial analysis. An-Chi Tsou, PhD, of CHBRP staff prepared the Policy Context and synthesized the individual sections into a single report. A subcommittee of CHBRP’s National Advisory Council (see previous page of this report) and a member(s) of the CHBRP Faculty Task Force, Nadereh Pourat, PhD, all of the University of California, Los Angeles, and Elizabeth Magnan, MD, PhD, of the University of California, Davis, reviewed the analysis for its accuracy, completeness, clarity, and responsiveness to the Legislature’s request.

CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

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Please direct any questions concerning this document to: California Health Benefits Review Program; MC 3116; Berkeley, CA 94720-3116, info@chbrp.org, or www.chbrp.org