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MANDATED BENEFIT REVIEW OF HOUSE BILL 984: AN ACT RELATIVE TO INSURANCE COVERAGE FOR PANDAS/PANS

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BENEFIT MANDATE OVERVIEW: H.B. 984: AN ACT RELATIVE TO INSURANCE COVERAGE FOR PANDAS/PANS

HISTORY OF THE BILL

The Joint Committee on Financial Services referred House Bill (H.B.) 984, "An Act relative to treatment for PANDAS/PANS," sponsored by Rep. Scibak of South Hadley in the 188th General Court (and submitted as H.B. 944 in the 189th General Court)[1] to the Center for Health Information and Analysis (CHIA) for review. Massachusetts General Laws, chapter 3, section 38C requires CHIA to review and evaluate the potential fiscal impact of each mandated benefit bill referred to the agency by a legislative committee.

WHAT DOES THE BILL PROPOSE?

H.B. 984 requires that health insurance plans "provide coverage for treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections [PANDAS] and pediatric acute-onset neuropsychiatric syndrome [PANS]. Said treatment shall include, but not be limited to, the use of Intravenous immunoglobulin (IVIG) therapy."

PANDAS/PANS

Obsessive-compulsive disorder (OCD) is an anxiety disorder characterized by unwanted thoughts and/or repetitive behaviors, which may include involuntary movements and/or vocalizations known as tics. PANS, or Pediatric Acute-onset Neuropsychiatric Syndrome, is a diagnosis applied to cases in which children experience an acute onset of OCD or tic disorders, but without a documented associated streptococcal infection. Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) is a diagnosis given to children who experience a sudden onset or worsening of OCD or tic disorders following streptococcal infection, and is considered a subset of PANS.

SUMMARY OF TREATMENT

At this time, no consensus treatment guidelines have been released for PANDAS or PANS. Current guidelines and recommendations call for treating acute infections, including strep, with standard antibiotic regimens, and the recommended treatment for chronic OCD and tic disorders continues to be psychotherapy and medications which target the symptoms of those disorders. A few studies of small groups of patients have found benefit from the prophylactic use of antibiotics, tonsillectomies, and immune system therapies such as plasmapheresis and/or IVIG specifically for the strep-related cases of PANDAS. However, researchers have called for additional studies before general conclusions can be drawn about the value of these specific treatments for PANDAS/PANS.

1 The 188th General Court of the Commonwealth of Massachusetts, House Bill 984, "An Act relative to treatment for PANDAS/PANS". Accessed 6 February 2015: https://malegislature.gov/Bills/188/House/H984. In the 189th General Court of the Commonwealth of Massachusetts, House Bill 944; accessed 16 March 2015: https://malegislature.gov/Bills/189/House/H944.

Until conclusive studies are released, entities such as the National Institute of Mental Health (NIMH) advise clinicians to balance the potential benefits and risks of additional treatments aimed at infection prevention (prophylactic antibiotics and tonsillectomies) and immune system modulation (plasmapheresis and IVIG). They caution providers that, due to risks and side effects, immune system therapies should be reserved for only the most severely ill PANDAS patients. Evidence regarding the diagnoses and treatment efficacy continues to evolve, and the results of additional studies, including an NIMH-funded clinical trial of IVIG for PANDAS, are anticipated in the next few years.

CURRENT COVERAGE

Responses to a recent survey of the largest insurance carriers in Massachusetts found that medication and psychotherapy treatments broadly used for strep infection, OCD, or tic disorders are already generally covered. Less conventional treatments, such as plasmapheresis and IVIG, are considered experimental when used to treat PANDAS/PANS, and are generally not covered.

COST OF IMPLEMENTING THE BILL

Requiring coverage for this benefit by fully-insured health plans would result in an average annual increase, over five years, to the typical member's monthly health insurance premiums of between $0.003 (0.001%) and $0.039 (0.008%) per year.

The Massachusetts Division of Insurance and the Health Connector are responsible for determining any potential state liability associated with the proposed mandate under Section 1311 of the Affordable Care Act (ACA).

PLANS AFFECTED BY THE PROPOSED BENEFIT MANDATE

Individual and group accident and sickness insurance policies, corporate group insurance policies, and HMO coverage issued pursuant to Massachusetts General Laws, as well as plans, self- and fully-insured, provided by the Group Insurance Commission (GIC) for public employees and their dependents, would be subject to this proposed mandate. The proposed mandate would apply to members covered under the relevant plans, regardless of whether they reside within the Commonwealth or merely have their principal place of employment in the Commonwealth.

PLANS NOT AFFECTED BY THE PROPOSED BENEFIT MANDATE

Self-insured plans (i.e., where the employer or policyholder retains the risk for medical expenses and uses a third party administrator or an insurer only to provide administrative functions), except for those managed under the GIC, are not subject to state-level health insurance benefit mandates. State health benefit mandates do not apply to Medicare and Medicare Advantage plans, the benefits of which are qualified by Medicare; this analysis excludes members of commercial fully-insured plans over 64 years of age. These mandates also do not apply to federally-funded plans including TRICARE (covering military personnel and dependents), the Veterans Administration, and the Federal Employee's Health Benefit Plan. Finally, this bill does not apply to Medicaid/MassHealth.

MEDICAL EFFICACY ASSESSMENT: TREATMENT FOR PANDAS/PANS

Massachusetts House Bill (H.B.) 984, submitted in the 188th General Court (and submitted as H.B. 944 in the 189th General Court), requires health insurance carriers to "provide coverage for treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections [PANDAS] and pediatric acute-onset neuropsychiatric syndrome [PANS]. Said treatment shall include, but not be limited to, the use of Intravenous immunoglobulin (IVIG) therapy."[1] M.G.L. c. 3 § 38C charges the Massachusetts Center for Health Information and Analysis (CHIA) with reviewing the medical efficacy of proposed mandated health insurance benefits. Medical efficacy reviews summarize current literature on the effectiveness and use of the mandated treatment or service, and describe the potential impact of a mandated benefit on the quality of patient care and the health status of the population.

CHRONIC OCD/TIC DISORDERS, PANDAS AND PANS

Obsessive-compulsive disorder is an anxiety disorder "characterized by recurrent, unwanted thoughts (obsessions) and/or repetitive behaviors (compulsions). Repetitive behaviors such as hand washing, counting, checking, or cleaning are often performed with the hope of preventing obsessive thoughts or making them go away."[2] The repetitive behaviors may include tics, which are involuntary movements and/or vocalizations.[3] As Figure 1 illustrates, PANS patients are a subset of those children with chronic OCD whose symptoms occurred severely and suddenly and span across several behavioral or neurological areas. Within this group of patients is another subset known as PANDAS, for whom the neurological symptoms coincide with or follow a streptococcal infection.

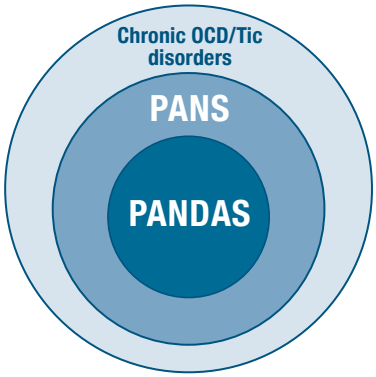


Figure 1: Relationship among Children with OCD, PANS, and PANDAS

PANDAS

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) is a diagnosis given to children who experience a sudden and dramatic onset or worsening of Obsessive Compulsive Disorder (OCD) and/or tic disorders following a streptococcal infection.[4] Cases of PANDAS were first described in medical literature in 1995[5] and formal diagnostic criteria were proposed in 1998.[6] Research continues to find evidence for this condition, although diagnosis is based on subjective criteria and not a confirmatory test.[7,8] Figure 2 outlines the diagnostic criteria and common neuropsychiatric symptoms associated with PANDAS. Figure 4 displays a diagnostic flow chart released by the PANDAS Physicians Network (PPN) that illustrates the difficulty with establishing a diagnosis for PANDAS.

FIGURE 2: PANDAS DIAGNOSTIC CRITERIA AND COMMON ASSOCIATED SYMPTOMS

Diagnostic Criteria[9,10]

- Presence of clinically significant obsessions, compulsions and/or tics.
- Unusually abrupt onset of symptoms or a relapsing-remitting course of symptom severity.
- Association with streptococcal infection (a positive throat culture for strep or history of scarlet fever).
- Prepubertal onset. (According to NIMH, this criterion is an arbitrary one, chosen because post-streptococcal reactions are rare after age 12. It allowed NIMH to study a more homogeneous group of patients, but investigators recognized that PANDAS could occur rarely among adolescents.)
- Association with other neuropsychiatric symptoms.

Additional Common Neuropsychiatric Symptoms[11]

- Severe separation anxiety (e.g., child can't leave parent's side or needs to sleep next to parent's bed).
- Generalized anxiety which may progress to episodes of panic and a "terror-stricken look".
- Motoric hyperactivity, abnormal movements, and a sense of restlessness.
- Sensory abnormalities, including hyper-sensitivity to light or sounds, distortions of visual perceptions, and occasionally, visual or auditory hallucinations.
- Concentration difficulties and loss of academic abilities, particularly in math and visual-spatial areas.
- Increased urinary frequency and a new onset of bed-wetting.
- Irritability (sometimes with aggression) and emotional lability. Abrupt onset of depression can also occur, with thoughts about suicide.
- Developmental regression, including temper tantrums, "baby talk", and handwriting deterioration (also related to motor symptoms).

While the exact mechanism that triggers PANDAS is currently unknown, researchers are investigating the theory that the syndrome is similar to a condition known as Sydenham chorea (SC),[12] a childhood neurological disorder characterized by "rapid, irregular, and aimless involuntary movements of the arms and legs, trunk, and facial muscles."[13] SC is the result of rheumatic fever, an autoimmune disorder triggered by a strep throat infection, which is caused by invading streptococcus bacteria.[14] In rheumatic fever, these strep bacteria "mimic" the cellular proteins of the heart valves, joints, or parts of the brain; as the body produces antibodies to fight the bacterial infection, the antibodies also begin to attack the child's valves, joints, or brain.[15] The result can be heart disease, arthritis, or SC, in which the strep bacteria mimic the part of the brain that controls movement and behavior.[16] Recent theories have proposed that PANDAS is a variant of SC, but that in PANDAS the condition results in predominantly psychiatric symptoms.[17] These studies further suggest that their similarities in cause and development may support similar treatments.[18]

PANS

In 2010, the diagnostic criteria for PANDAS were modified to identify cases in which children experienced an acute onset of OCD or tic disorders, but for which no association with a streptococcal infection could be documented.[19] This newer and broader category is known as PANS, or Pediatric Acute-onset Neuropsychiatric Syndrome. Again, while research studies continue to support the diagnosis, confirmation of the condition is based on subjective evaluation.[20,21,22] PANS is known as a "diagnosis of exclusion", meaning that to diagnose PANS, clinicians must rule out other neurologic or medical disorders.[23] While PANS symptoms overlap with other psychiatric conditions, the diagnosis is differentiated by the sudden and severe onset of symptoms in multiple areas.[24] The first consensus statement from researchers and clinicians on the recommended diagnostic evaluation for PANS was released in 2013.[25] Figure 3 outlines the diagnostic criteria and neuropsychiatric symptoms for PANS. Figure 5 displays a diagnostic flow chart released by the PANDAS Physicians Network that illustrates the difficulty with diagnosing PANS.

FIGURE 3: PEDIATRIC ACUTE-ONSET NEUROPSYCHIATRIC SYNDROME

Diagnostic Criteria[26]

- Abrupt, dramatic onset of obsessive-compulsive disorder or severely restricted food intake.[27]
- Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder, or others.
- Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least two of seven categories (listed right).

Additional Common Neuropsychiatric Symptoms[28]

- Anxiety (particularly, separation anxiety)
- Sensory or motor abnormalities
- Deterioration in school performance
- Somatic signs and symptoms, including sleep disturbances, bedwetting or urinary frequency
- Emotional lability (extreme mood swings) and/or depression
- Irritability, aggression and/or severely oppositional behaviors
- Behavioral (developmental) regression (examples, talking baby talk, throwing temper tantrums, etc)

TREATMENT FOR PANDAS/PANS

Currently, the first treatment given for PANDAS/PANS includes antibiotics for any lingering bacterial infection, as well as psychotherapy and medication treatment for associated OCD and/or tic disorder.[29] While no consensus treatment guidelines yet exist for these syndromes, the PANDAS Physicians Network has recommended treatment based on patient symptom severity (Figure 6).[30]

For most patients, eliminating the strep infection is the most effective treatment for PANDAS acute episodes.[31,32] And while a throat infection is the easiest strep infection to treat, strep can also rarely cause infection outside of the throat, making it more difficult to identify and eliminate, and requiring a longer course of antibiotic treatment.[33,34] Similarly, if a child is diagnosed with PANS triggered by an infection other than strep, treatment of that infection "may be useful in reducing symptom severity of the OCD and other neuropsychiatric symptoms."[35] Both PANDAS and PANS are episodic conditions, and patients are expected to experience periods of symptom reduction or remission with the disorders.[36]

Effective treatments for the symptoms of OCD and tic disorders include psychotherapy and/or medications.[37,38]

A recent meta-analysis also showed that, for children with OCD, combining cognitive behavioral therapy (CBT) with medication, especially selective serotonin re-uptake inhibitors (SSRIs), was better than the use of either of these treatments individually, and that either of these is better than no treatment or placebo.[39,40]

The responses to a recent survey of the largest insurance carriers in Massachusetts found that treatments more broadly used for strep infections, OCD, or tic disorders are already generally covered, and will therefore not be evaluated as part of this analysis. Instead, this report will focus on treatments specific to PANDAS/PANS. Researchers are currently evaluating several treatments for these syndromes, including longer-term use of antibiotics, tonsillectomy, and immunomodulatory therapies such as plasma exchange (plasmapheresis) and intravenous immunoglobulin (IVIG) aimed at modifying a patient's immune response.[41,42] One recent study concluded that "[b]ecause of the wide variety of medical and psychiatric symptoms, youth with PANS [including PANDAS] may require a multidisciplinary team for adequate care management."[43]

Research regarding the effectiveness of treatment for either PANDAS or PANS is not yet complete, nor is it conclusive. Most studies have been directed at PANDAS, as PANS is a more recently-defined syndrome. Given this, the National Institute of Mental Health (NIMH) reports only that the treatment information which they outline for PANDAS "may prove useful for PANS as well."[44] This general statement, in the absence of research studies directed more broadly at PANS, does not specify which treatments may be effective. The NIMH goes on to state that "immune-based therapies should be used only in cases where it is clear that the neuropsychiatric symptoms are related to an autoimmune response (as in PANDAS and many cases of PANS)."[45] This lack of specificity and the general lack of evidence about the effectiveness of immunomodulatory treatments for PANS precludes drawing conclusions about effectiveness.

Antibiotics

Beyond the use of antibiotics to treat an identified bacterial infection, the NIMH states that some clinicians have observed "significant improvement in the OCD and other neuropsychiatric symptoms following [antibiotic] treatment [in the absence of an identifiable infection]."[46] However, the agency points out that these case reports "need to be confirmed by a controlled treatment trial,"[47] and that currently "there isn't enough evidence to recommend the long-term use of antibiotics" for the treatment of PANDAS/PANS when no infection is present.[48] A recent study found some "nonstatistically significant" improvement in tic and OCD symptoms for patients using a specific antibiotic regimen, suggesting that a larger study of this treatment may be warranted.[49] Further, a recently-completed study from the National Institutes of Health (NIH) is intended to evaluate whether the use of antibiotics can reduce symptom severity for both PANDAS and PANS even in the absence of an identified infection; results of this study have not yet been released.[50]

The use of antibiotics as a prophylaxis (protective treatment) to prevent strep infections in children who have had previous infection may be helpful in avoiding future PANDAS episodes. Studies have shown that prophylactic antibiotic use is beneficial to patients with rheumatic fever and Sydenham chorea, two similar conditions, and two clinical trials have found that "prophylaxis were found to be effective in decreasing streptococcal infections and neuropsychiatric symptom exacerbations among children in the PANDAS subgroup."[51,52] However, these studies were small, and additional research is needed "to provide definitive support for the use of prophylactic antibiotics in PANDAS."[53] NIMH advises clinicians to balance the benefits of preventing strep infections against the known risk of antibiotic administration, and advises clinicians to follow rheumatic fever guidelines when using this treatment method.[54]

Tonsillectomy

Tonsillectomies are also considered for some children with PANDAS for whom antibiotic use is not effective at treating strep infection, or to prevent future infections from triggering neuropsychiatric symptoms. On its PANDAS webpage, NIMH states that "NIH does not recommend tonsillectomies for children with PANDAS, as there is no evidence that they are helpful."[55] However, a new study published in January 2015 that examined the role of tonsillectomy in the treatment of PANDAS concluded that the specific group of patients in the study "whose neuropsychiatric symptoms did not respond sufficiently to antibiotics may have gained benefit from tonsillectomy."[56] At this time, however, no consensus treatment guidelines exist regarding this approach, and specific studies of this treatment have not yet been conducted for PANS.[57]

Plasmapheresis and IVIG

Going beyond more conventional treatments, certain immunomodulatory therapies are aimed at preventing antibodies from attacking a PANDAS or PANS patient's own immune system. One such treatment, plasmapheresis, separates the liquid in the blood, or plasma, where the antibodies are located, removing it from the body and replacing it with donor plasma or a plasma substitute.[58,59] In another, IVIG, a concentrated solution of antibodies from a large group of donors is infused intravenously into a patient.[60] These treatments were shown in a 1999 study to lessen symptom severity in children with tic disorders and OCD triggered by infection.[61] The researchers stated, though, that "[f]urther studies are needed to determine the active mechanism of these interventions, and to determine which children with OCD and tic disorders will benefit from immunomodulatory therapies."[62]

NIMH cautions that plasmapheresis and IVIG "should be reserved for severely ill patients, and administered by a qualified team of health care professionals," as these treatments carry infection risks associated with invasive procedures, as well as side effects including severe headaches, dizziness, nausea, and vomiting.[63] Further, the agency states that these therapies should only be administered in cases where the neuropsychiatric symptoms are directly related to an autoimmune response.[64] The PANDAS Physicians Network states that:

> Although plasmapheresis and IVIG appear to provide the best long-term outcomes, they are expensive and involve risks which are not warranted in the treatment of mild-moderate cases of PANDAS; even for more severely ill patients, their use may be reserved for treatment of patients who fail to respond to antibiotics and other non-invasive therapies.[65]

A recent case series reviewed the efficacy of IVIG for children with PANDAS. Despite the limitations of the study, including its small size, selective nature, and reliance on patient and parent self-reported symptoms, the researchers found the treatment demonstrated benefits even for those "who had been symptomatic for several years prior to treatment." All of the patients had "failed" the use of prior therapies, including antibiotics, "suggesting that the immunomodulatory effects of IVIG were responsible for the symptomatic improvements."[66] IVIG treatment for PANDAS differs from its use with other autoimmune disorders, which often require multiple doses. In PANDAS, patients may respond to a single treatment of IVIG which serves to inactivate the patient's antibodies which were attacking the patient's own cells, rather than the bacterial infection.[67] Once these antibodies are regulated, the PANDAS symptoms begin to subside. Currently, NIMH is funding a multi-site, double-blind, placebo-controlled clinical trial of IVIG as a treatment for PANDAS; final data collection for this study is anticipated for December 2015.[68]

And while studies are still underway, the American Society of Apheresis now lists plasmapheresis as a "first line"[69] therapy for PANDAS.[70,71] While this professional organization of physicians, scientists, and allied health professionals recommends plasmapheresis as the first treatment for PANDAS given as part of a standard set of treatments, other clinicians recommend a more conservative approach to its use. For example, recent retrospective case review of the use of plasmapheresis for PANDAS concluded that it is "an invasive medical intervention that should be reserved for treatment of children and adolescents who are severely affected by PANDAS. In such patients, it appears to be a safe, well-tolerated, and beneficial treatment option."[72] This conclusion is further echoed by the PANDAS Physicians Network, which states that as an invasive procedure with associated risks, plasmapheresis is not deemed appropriate treatment for children with mild to moderate symptoms, and should be reserved for patients with severe to extreme symptoms.[73]

Again, most research to date has been focused on PANDAS, the syndrome identified first, and not PANS. While the NIMH has stated that plasmapheresis and IVIG may "prove useful for PANS as well," two studies focused more broadly on chronic OCD/tic disorders found that the use of immunomodulatory therapies may not be effective for non-PANDAS cases. A study of the use of plasmapheresis for children with chronic OCD not triggered by strep infection found no benefit of the treatment;[74] similarly, IVIG was found to be ineffective in treating patients with non-PANDAS tic disorders.[75] These studies have led NIMH to suggest that "plasma exchange or IVIG is not helpful for children who do not have strep triggered OCD or tics."[76] However, as Figure 1 illustrates, chronic OCD/tic disorders may or may not be inclusive of PANS cases, making it difficult to draw conclusions about these treatments for PANS specifically.

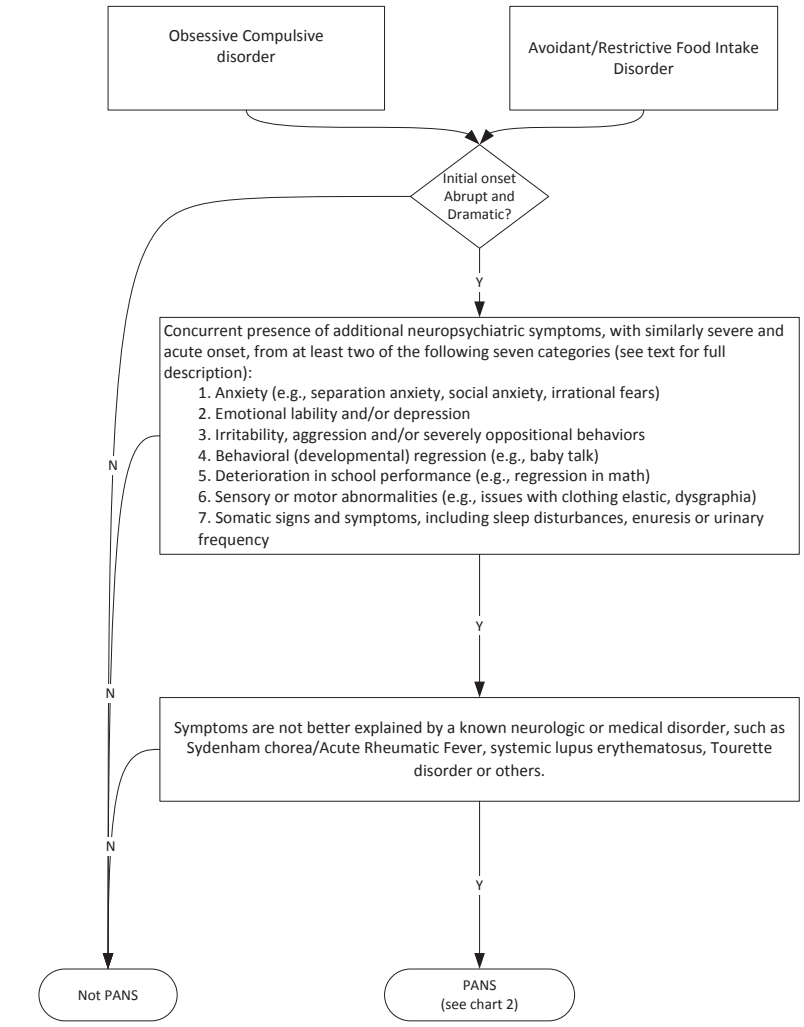
SUMMARY OF TREATMENT

Research on PANDAS/PANS continues to evolve as diagnostic groups are more clearly defined and treatment methods tested. No consensus treatment guidelines have yet been developed, but groups such as the PANDAS Physicians Network have released information on the risks and benefits of different treatment approaches based on patient symptom severity.

At this time, guidelines and recommendations for treating acute infections, including strep, with standard antibiotic regimens remain unchanged, and recommended treatment for chronic OCD and tic disorders continues to be psychotherapy and medications which target symptoms of those disorders. A few studies of small groups of patients have found benefit from the prophylactic use of antibiotics, tonsillectomies, and immunomodulatory therapies such as plasmapheresis and/or IVIG specifically for the strep-related cases of PANDAS. In the absence of studies specifically researching the effectiveness of other treatments for non-strep related (non-PANDAS) PANS, the NIMH has issued a general statement that treatment information for PANDAS "may prove useful for PANS as well." However, it is not possible to draw clear conclusions about immunomodulatory therapies for PANS at this time. In general, researchers have called for additional studies before general conclusions can be drawn regarding the effectiveness of any specific treatments for PANDAS or PANS.

Until conclusive studies are released, groups such as NIMH and PPN advise clinicians to balance the potential benefits and risks of additional treatments aimed at infection prevention (prophylactic antibiotics and tonsillectomies) and immune system modulation (plasmapheresis and IVIG). Both groups caution providers that, due to risks and side effects, immunomodulatory therapies should be reserved for only the most severely ill PANDAS patients. Evidence regarding the diagnoses and treatment efficacy continues to evolve, and the results of additional studies, including the NIMH-funded clinical trial of IVIG for PANDAS, are anticipated in the next few years.

FIGURE 4: DIAGNOSTIC FLOW CHART FOR PANS[77]



Common Obsessive Compulsive symptoms in children are:

- Doorway rituals
- Contamination fears
- Compulsive hand washing
- Counting/Touching ritual
- Symmetry issues
- Excessive confessing

To be considered for PANS, the child must meet the DSM 5 criteria for OCD or be diagnosed with avoidant or restrictive food intake disorder.

Abrupt and dramatic onset is defined as significant behavioral change that is typically isolated to a particular day or week. Typical presentation has a shift of >16 pts in CYBOC scores. Unlike traditional OCD or ED, many parents can name the time/day when onset occurs in their child

In children, daytime urinary frequency (with no apparent UTI) is a common first clinical complaint.

The diagnostic work-up of patients suspected of PANS must be comprehensive enough to rule out these and other relevant disorders. The nature of the co-occurring symptoms will dictate the necessary assessments, which may include MRI scan, lumbar puncture, electroencephalogram or other diagnostic tests.

Swedo SE, Leckman JF, Rose NR. From research subgroup to clinical syndrome: modifying the PANDAS criteria to describe PANS (pediatric acute-onset neuropsychiatric syndrome). Pediatrics & Therapeutics 2012, 2:2. On-line article available at: http://dx.doi.org/10.4172/2161-0665.1000113

FIGURE 5: DIAGNOSTIC FLOW CHART FOR PANDAS[78]

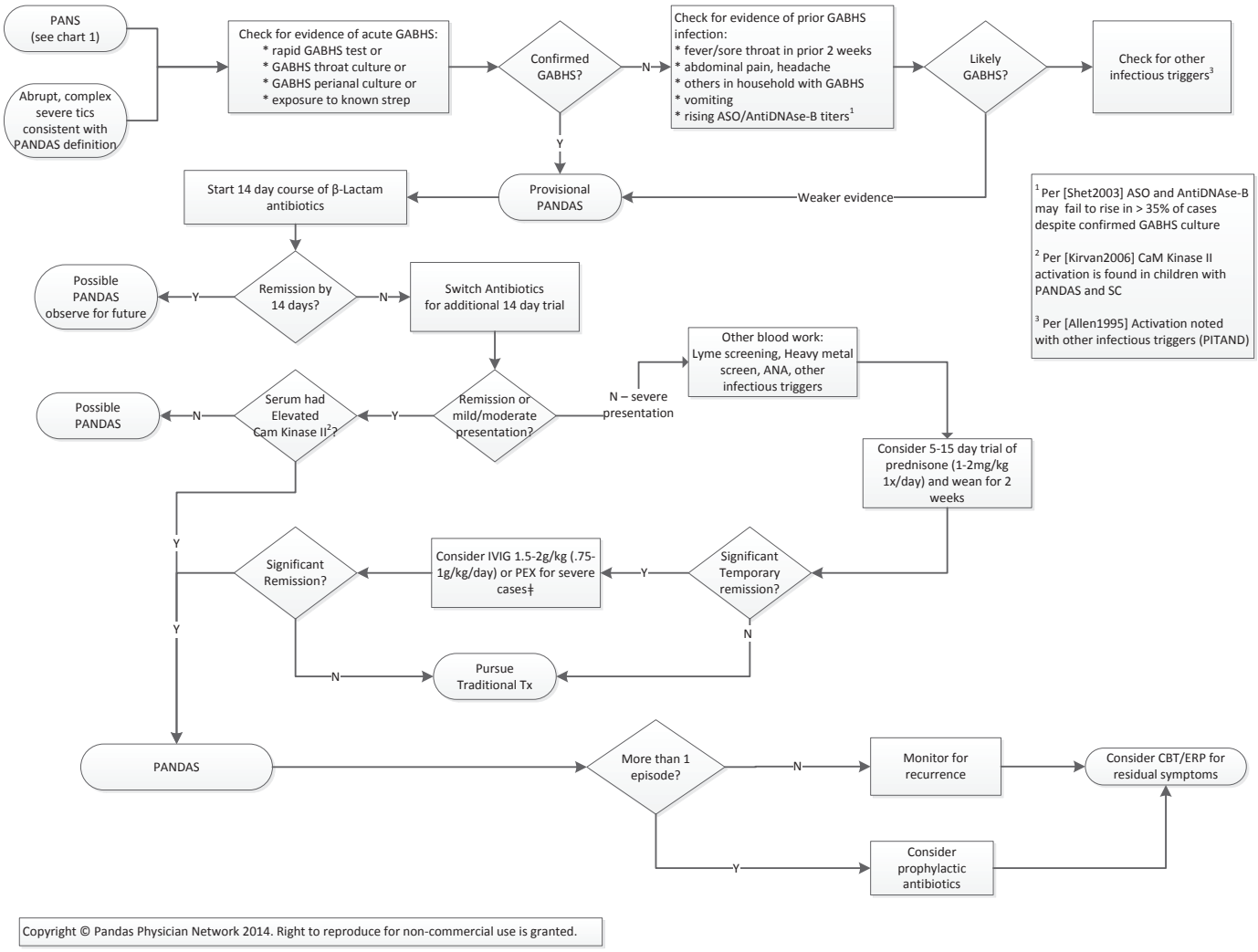


FIGURE 6: GUIDE TO ASSESSING THE RISK AND BENEFITS OF IVIG AND PLASMAPHERESIS

The PANDAS Physicians Network produced the following guide to assessing the risk and benefits of IVIG and Plasmapheresis for treating PANDAS.[79]

SYMPTOM SEVERITY	TREATMENT
Severe-Extreme Illness ■ Neuropsychiatric symptoms have life-threatening consequences. Examples: • Significant weight loss >10-15% of body mass due to anorexia or obsessional food/eating restrictions. • Extreme impulsivity and behavioral regression. • Suicidal ideation or self-injurious behavior. ■ Anxiety and obsessional fears occupy >80% of waking hours, preventing children from activities of daily living (accomplishing tasks such as showering and toileting, attending school, etc.). May include extreme irritability, increased aggression and emotional lability, dramatic personality change.	■ Immediate therapeutic dose of antibiotics ■ Plasmapheresis may be first-line treatment if available ■ IVIG as alternative ■ Supportive therapy ■ Cognitive behavioral therapy ■ Psychotropic medications such as SSRIs (must be started at extremely low dose and slowly tapered due to significant risks of side effects) ■ Treatment followed with prophylactic dose of antibiotics
Moderate Illness ■ Neuropsychiatric symptoms have life-threatening consequences. Examples: • Significant weight loss >10-15% of body mass due to anorexia or obsessional food/eating restrictions. • Extreme impulsivity and behavioral regression. • Suicidal ideation or self-injurious behavior. ■ Anxiety and obsessional fears occupy 50-70% of waking hours, cause significant interference with daily activities, but do not overwhelm them continuously. ■ Ancillary symptoms are impairing but not incapacitating.	■ Immediate therapeutic dose of antibiotics ■ IVIG is preferred therapy if antibiotic treatment fails* ■ Cognitive behavioral therapy ■ Supportive therapy ■ Psychotropic medications such as SSRIs (must be started at extremely low dose and slowly tapered due to significant risks of side effects) ■ Treatment followed with prophylactic dose of antibiotics * Some clinicians recommend a diagnostic "steroid burst" to determine whether or not IVIG therapy will be beneficial. Treatment may produce significant symptomatic improvement, although symptoms will return after cessation of the steroids. A positive response to steroids is a good indication that IVIG therapy will be helpful, although a tepid response is not a predictor of IVIG failure.
Mild Illness ■ Obvious impairments limited to certain situations or settings. ■ Anxiety and obsessional fears occupy 1-2 waking hours, and are not overwhelming. ■ Symptoms may cause minor disruptions but are manageable with reasonable accommodations (troubled but tolerable).	■ Immediate therapeutic dose of antibiotics ■ Treatment followed with prophylactic dose of antibiotics

ENDNOTES

1 The 188th General Court of the Commonwealth of Massachusetts, House Bill 984, "An Act relative to treatment for PANDAS/PANS". Accessed 6 February 2015: https://malegislature.gov/Bills/188/House/H984. In the 189th General Court of the Commonwealth of Massachusetts, House Bill 944; accessed 16 March 2015: https://malegislature.gov/Bills/189/House/H944.

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CENTER FOR HEALTH
INFORMATION AND ANALYSIS

APPENDIX

Actuarial Assessment of House Bill 984 Submitted to the 188th General Court: "An Act relative to insurance coverage for PANDAS/PANS"

Prepared for
Commonwealth of Massachusetts
Center for Health Information and Analysis

May 2015

Prepared by
Compass Health Analytics, Inc.

Actuarial Assessment of House Bill 984
Submitted to the 188th General Court:
"An Act relative to insurance coverage for PANDAS/PANS"

Table of Contents

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Actuarial Assessment of House Bill 984
"An Act relative to insurance coverage for PANDAS/PANS"

Executive Summary

Massachusetts House Bill 984 (H.B. 984), as drafted for the 188th General Court (and submitted as House Bill 944 in the 189th General Court), would require that commercial health insurance plans "provide coverage for treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections [PANDAS] and pediatric acute-onset neuropsychiatric syndrome [PANS]. Said treatment shall include, but not be limited to, the use of Intravenous immunoglobulin (IVIG) therapy."[1] Massachusetts General Laws (M.G.L.) c. 3 § 38C charges the Massachusetts Center for Health Information and Analysis (CHIA) with reviewing the potential impact of proposed mandated health care insurance benefits on the premiums paid by businesses and consumers. CHIA has engaged Compass Health Analytics, Inc. to provide an actuarial estimate of the effect the proposed law would have on the cost of health care insurance in Massachusetts.

Background

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) is a diagnosis given to children who experience a sudden and dramatic onset or worsening of obsessive compulsive disorder (OCD) and/or tic disorders following a streptococcal infection.[2] Cases of PANDAS were first described in medical literature in 1995[3] and formal diagnostic criteria were proposed in 1998.[4] Researchers continue to find evidence for this condition, although diagnosis is based on subjective criteria and not a confirmatory test.[5,6] In 2010 the diagnostic criteria for PANDAS was modified to identify cases in which children experienced an acute onset of OCD or tic disorders but with no documented associated streptococcal infection.[7] This newer and broader category is known as PANS, or Pediatric Acute-onset Neuropsychiatric Syndrome. While research studies continue to support the diagnosis, confirmation of the condition is based on subjective evaluation.[8,9,10]

Children diagnosed with PANDAS/PANS are treated with antibiotics for bacterial infection and with psychotherapy and medication for associated OCD and/or tic disorders.[11] No consensus treatment guidelines have yet been developed, but researchers are evaluating other treatments for these syndromes, including extended use of antibiotics, tonsillectomy, and more invasive therapies such as plasma exchange (plasmapheresis) and IVIG aimed at modifying a patient's immune response.[12,13]

In response to a recent survey of insurance carriers in Massachusetts, all reported coverage for medication and psychotherapy treatments broadly used for strep infections, OCD, or tic disorders. However, plasmapheresis and IVIG treatments are considered experimental when used to treat PANDAS/PANS, and are generally not covered. H.B. 984's requirement that commercial carriers cover IVIG and other treatment of PANDAS/PANS modifies existing coverage by commercial carriers.

Analysis

Compass estimated the impact of H.B. 984 by performing the following steps.

Analyze service delivery impact

- Estimate the prevalence of OCD and/or tic disorders among children.
- Estimate the prevalence of PANDAS/PANS among children with OCD and/or tic disorders.
- Estimate the number of fully commercially insured children in Massachusetts with PANDAS/PANS.
- Estimate the distribution of treatment modalities among children with PANDAS/PANS under the proposed mandate, resulting in a set of probabilities that any one PANDAS/PANS patient will receive each of the various treatments.
- Multiply the treatment type probabilities by the estimated number of fully-insured children with PANDAS/PANS, and multiply by the estimated number of lifetime treatments per user, to calculate the total lifetime number of treatments (by type).
- Divide the lifetime treatments by 18 to approximate the number of annual treatments.
- Using the Massachusetts All Payer Claim Database (APCD) and available literature estimate annual treatment cost for each treatment modality that contributes to the incremental cost of the mandate (i.e., those not currently covered).

Calculate the impact on premiums of projected spending

- Multiply the incremental treatment cost per user by the estimated number of annual treatments for PANDAS/PANS to calculate incremental medical spending. Divide by the corresponding commercial fully-insured membership to get per member per month (PMPM) medical expense.
- Estimate the impact of insurer retention (administrative costs and profit) on premiums.
- Estimate the fully-insured Massachusetts population under age 65, projected for the next five years (2016 to 2020).
- Project the estimated cost over the next five years.

Factors affecting the analysis include a reliance on assumptions about the prevalence rate of PANDAS/PANS and the estimated cost per person per year to treat the condition under the provisions of H.B. 984. These uncertainties are addressed by modeling a range of assumptions within reasonable judgment-based ranges.

Summary results

Table ES-1 summarizes the effect of H.B. 984 as drafted for the 188th General Court on premiums for fully-insured plans, averaged over five years. Note that the effective date of the relevant provisions is assumed to be January 1, 2016.

The low scenario impact is small at $77,000 per year on average, and is due to the low prevalence rate and a smaller number of those children with PANDAS/PANS using the more expensive treatment options. The high scenario has average cost of $1.1 million per year, and reflects an estimate that a higher portion (1.0 percent) of the entire population of children will get PANDAS/PANS. The mid-scenario has average annual costs of $387,000, or an average of 0.003 percent of premium.

Finally, the impact of the proposed mandate on any one individual, employer-group, or carrier may vary from the overall results depending on the current level of benefits each receives or provides, and on how the benefits will change under the mandate.

Table ES-1:
Summary Results

	2016	2017	2018	2019	2020	Weighted Average	5 Yr Total
Members (000s)	2,329	2,305	2,279	2,253	2,226		
Medical Expense Low ($000s)	$46	$67	$69	$72	$75	$70	$329
Medical Expense Mid ($000s)	$230	$335	$345	$359	$372	$349	$1,642
Medical Expense High ($000s)	$641	$931	$959	$998	$1,035	$971	$4,564
Premium Low ($000s)	$51	$74	$77	$80	$83	$77	$364
Premium Mid ($000s)	$255	$371	$382	$398	$412	$387	$1,819
Premium High ($000s)	$710	$1,031	$1,063	$1,105	$1,147	$1,076	$5,056
PMPM Premium Low	$0.003	$0.003	$0.003	$0.003	$0.003	$0.003	$0.003
PMPM Premium Mid	$0.013	$0.013	$0.014	$0.015	$0.015	$0.014	$0.014
PMPM Premium High	$0.036	$0.037	$0.039	$0.041	$0.043	$0.039	$0.039
Estimated Monthly Premium	$473	$487	$501	$515	$530	$487	$487
Premium % Rise Low	0.001%	0.001%	0.001%	0.001%	0.001%	0.001%	0.001%
Premium % Rise Mid	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%
Premium % Rise High	0.008%	0.008%	0.008%	0.008%	0.008%	0.008%	0.008%

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Actuarial Assessment of House Bill 984: "An Act relative to insurance coverage for PANDAS/PANS"

1. Introduction

Massachusetts House Bill 984 (H.B. 984), as drafted for the 188th General Court (and submitted as House Bill 944 in the 189th General Court), would require commercial health insurance plans to cover "treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections [PANDAS] and pediatric acute-onset neuropsychiatric syndrome [PANS]. Said treatment shall include, but not be limited to, the use of Intravenous immunoglobulin (IVIG) therapy."[1] Massachusetts General Laws (M.G.L.) c. 3 § 38C charges the Massachusetts Center for Health Information and Analysis (CHIA) with reviewing the potential impact of proposed mandated health care insurance benefits on the premiums paid by businesses and consumers. CHIA has engaged Compass Health Analytics, Inc. to provide an actuarial estimate of the effect the proposed law would have on the cost of health care insurance in Massachusetts.

Assessing the impact of this proposed mandate on premiums entails analyzing the incremental effect of the proposed law on spending by insurance plans. This in turn requires comparing spending under the provisions of the law to spending under current statutes and current benefit plans for the relevant services.

Section 2 of this analysis outlines the provisions of the bill. Section 3 summarizes the methodology used for the estimate. Section 4 discusses important considerations in translating the bill's language into estimates of its incremental impact on health care costs and steps through the calculations. Section 5 summarizes the results.

2. Interpretation of House Bill 984

The following subsections describe the provisions of H.B. 984, as drafted for the 188th General Court.

2.1. Plans affected by the proposed mandate

H.B. 984 would amend the statutes that regulate insurers providing health insurance in Massachusetts, applying the mandate to all fully-insured coverage by the full set of commercial insurance licenses and all plans offered by the Group Insurance Commission, as listed below.

- Section 1: Insurance for persons in service of the Commonwealth (creating M.G.L. c. 32A, § 17L)
- Section 2 Accident and sickness insurance policies (creating M.G.L. c. 175, § 47EE)
- Section 3: Contracts with non-profit hospital service corporations (creating M.G.L. c. 176A, § 8FF)

- Section 4 Certificates under medical service agreements (creating M.G.L. c. 176B, § 4GG)
- Section 5: Health maintenance contracts (creating M.G.L. c. 176G, § 4Y)

This analysis assumes the bill proposes coverage for members under the relevant Massachusetts-licensed plans regardless of whether they reside within the Commonwealth or merely have their principal place of employment in the Commonwealth.

Self-insured plans, except for those managed by the GIC, are not subject to state-level health insurance benefit mandates. State mandates do not apply to Medicare or Medicare Advantage plans, the benefits of which are qualified by Medicare. This analysis assumes that this mandate does not affect Medicare extension/supplement plans even to the extent they are regulated by state law (and because the condition the bill addresses is defined only for children). Finally, this analysis does not apply to Medicaid/MassHealth.

This analysis assumes the proposed legislation, if enacted, would be effective for policies issued or renewed on or after January 1, 2016.

2.2. Covered services

PANDAS/PANS

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) is a diagnosis given to children who experience a sudden and dramatic onset or worsening of obsessive compulsive disorder (OCD) and/or tic disorders following a streptococcal infection.[2] Cases of PANDAS were first described in medical literature in 1995[3] and formal diagnostic criteria were proposed in 1998.[4] Research continues to find evidence for this condition, although diagnosis is based on subjective criteria and not a confirmatory test.[5,6]

In 2010 the diagnostic criteria for PANDAS was modified to identify cases in which children experienced an acute onset of OCD or tic disorders, but with no documented associated streptococcal infection.[7] This newer and broader category is known as PANS, or Pediatric Acute-onset Neuropsychiatric Syndrome. Again, while research studies continue to support the diagnosis, confirmation of the condition is based on subjective evaluation.[8,9,10] PANS is known as a "diagnosis of exclusion," meaning that to diagnose PANS clinicians must rule out other neurologic or medical disorders.[11] While PANS symptoms overlap with other psychiatric conditions the diagnosis is differentiated by the sudden and severe onset of symptoms in multiple areas.[12] The first consensus statement from researchers and clinicians on the recommended diagnostic evaluation for PANS was released in 2013.[13] Both PANDAS and PANS are episodic conditions, such that patients are expected to experience periods of symptom reduction or remission.[14]

Treatments for PANDAS/PANS

Children diagnosed with PANDAS/PANS are treated with antibiotics for bacterial infection and with psychotherapy and medication for associated OCD and/or tic disorders.[15] No consensus treatment guidelines have yet been developed, but researchers are evaluating other treatments for these

syndromes, including extended use of antibiotics, tonsillectomy, and more invasive therapies such as plasma exchange (plasmapheresis) and IVIG aimed at modifying a patient's immune response.[16,17]

To date, some studies based on small sample sizes find benefit from these other treatments. Most researchers have called for additional studies, and entities such as the National Institute of Mental Health (NIMH) continue to recommend treatment for the symptoms of acute infections, OCD, and tic disorders as primary treatment for PANDAS/PANS. Regarding additional treatments aimed at infection prevention (long-term antibiotics and tonsillectomies) and immune system modulation (plasmapheresis and IVIG), NIMH advises clinicians to balance the potential benefits and risks of these treatments. It cautions providers that, due to risks and side effects, immune system therapies should be reserved for only the most severely ill PANDAS patients. Evidence regarding the diagnoses and treatment efficacy continues to evolve, and the results of additional studies, including an NIMH-funded clinical trial of IVIG for PANDAS, are anticipated in the next few years.

2.3. Carrier coverage

In responses to a recent survey of ten of the largest insurance carriers in Massachusetts, all reported coverage for medication and psychotherapy treatments broadly used for strep infections, OCD, or tic disorders. However, plasmapheresis and IVIG treatments are considered experimental when used to treat PANDAS/PANS and are generally not covered by the top ten carriers.

H.B. 984 requires commercial carriers to provide coverage for the treatment of PANDAS/PANS, including, but not limited to, the use of IVIG. Requiring this and other treatments specifically for PANDAS/PANS modifies existing coverage by commercial carriers.

2.4. Existing laws affecting the cost of H.B. 984

This analysis has uncovered no current Massachusetts insurance mandates regarding insurance coverage for the treatment of PANDAS/PANS. In addition, no existing federal insurance mandates related to the specific subject matter of this bill have been identified.

3. Methodology

3.1. Overview

Analyzing H.B. 984's impact on premiums required estimating the prevalence of PANDAS/PANS, the distribution of current treatment modalities among children with the conditions, and the cost per treatment for each modality. Combining these components resulted in a baseline estimate of the incremental effect on premiums of the proposed mandate, which Compass then projected over the five years following the assumed implementation date of the law (2016 through 2020).

3.2. Steps in the analysis

The general approach outlined above was executed in the following steps.

Analyze service delivery impact

- Estimate the prevalence of OCD and/or tic disorders among children.
- Estimate the prevalence of PANDAS/PANS among children with OCD and/or tic disorders.
- Estimate the number of commercial fully-insured children in Massachusetts with PANDAS/PANS.
- Estimate the distribution of treatment modalities among children with PANDAS/PANS under the proposed mandate, resulting in a set of probabilities that any one PANDAS/PANS patient will receive each of the various treatments.
- Multiply the treatment type probabilities by the estimated number of fully-insured children with PANDAS/PANS, and multiply by the estimated number of lifetime treatments per user, to calculate the total lifetime number of treatments (by type).
- Divide the lifetime treatments by 18 to approximate the number of annual treatments.
- Using the Massachusetts All Payer Claim Database (APCD) and available literature estimate annual treatment cost for each treatment modality that contributes to the incremental cost of the mandate (i.e., those not currently covered).

Calculate the impact on premiums of projected spending

- Multiply the incremental treatment cost per user by the estimated number of annual treatments for PANDAS/PANS to calculate incremental medical spending. Divide by the corresponding commercial fully-insured membership to get per member per month (PMPM) medical expense.
- Estimate the impact of insurer retention (administrative costs and profit) on premiums.
- Estimate the fully-insured Massachusetts population under age 65, projected for the next five years (2016 to 2020).
- Project the estimated cost over the next five years.

Section 4 describes these steps in more detail.

3.3. Data sources

The primary data sources used in the analysis were:

- Information gathered from clinicians
- Information from a survey administered to private health insurance carriers in Massachusetts

- Academic literature, published reports, and population data, cited as appropriate
- Massachusetts insurer claim data from CHIA's Massachusetts All Payer Claim Database (APCD) for calendar years 2009 to 2012, for plans covering the majority of the under-65 fully insured population subject to the mandate

3.4. Limitations

This analysis relies primarily on an assessment of the prevalence rate of PANDAS/PANS and the estimated cost per person per year to treat the condition under the provisions of H.B. 984. The estimates draw on published prevalence rates and 2012 statewide data on cost per treatment for incremental (not currently covered) modalities when used for other covered conditions. These costs are adjusted to reflect treatment protocols for PANDAS/PANS.

This estimation includes some uncertainty because of limited information on the prevalence of PANDAS/PANS, a subset of children with OCD and/or tic disorders. Published studies on prevalence of OCD and/or tic disorders relative to the entire population present a range of results. Further, there is insufficient data to pinpoint prevalence of PANDAS/PANS among children with OCD and/or tic disorders, in large part because the diagnostic criteria are subjective and have yet to be codified in the International Statistical Classification of Diseases and Related Health Problems (ICD) or the Diagnostic and Statistical Manual of Mental Disorders (DSM), the standard medical and psychiatric diagnostic code sets, respectively.

Uncertainty is also present in the cost per treatment and how many PANDAS/PANS patients will be treated under each of the available treatment types. The treatments required by the proposed mandate are considered experimental when applied to PANDAS/PANS and are generally not covered by commercial carriers; introducing insurance coverage may change treatment patterns and raise utilization for treatments in unpredictable ways.

These uncertainties are addressed by modeling a range of assumptions within reasonable judgment-based ranges. The more detailed step-by-step description of the estimation process below further addresses these uncertainties as appropriate.

4. Analysis

This section describes the calculations outlined in the previous section in more detail. The analysis includes development of a best estimate "middle-cost" scenario, as well as a low-cost scenario using assumptions that produced a lower estimate, and a high-cost scenario using more conservative assumptions that produced a higher estimated impact.

Sections 4.1 and 4.2 below describe the steps used to calculate the number of children with PANDAS/PANS. Sections 4.3 to 4.5 describe the types of treatment, how those treatments are expected to be distributed, the number of treatments per year, and the cost per treatment. Sections 4.6 to 4.9 discuss the incremental cost calculation and the projection over the 2016 to 2020 reporting period.

4.1. Prevalence of children with OCD and/or tic disorders

The impact of H.B. 984 on premiums stems from requiring carriers to cover treatment for PANDAS/PANS, a diagnosis given to children who experience a dramatic onset or worsening of OCD and/or chronic tic disorders, and quantifying that impact begins with an estimate of children with those conditions. Recent epidemiological studies found that the lifetime prevalence of pediatric OCD in the United States is between one and four percent of all children.[18] A 2014 study concluded that the best estimate of prevalence for chronic tic disorders in school-age children is likely between 0.4 percent and 0.8 percent.[19] This analysis assumes the same prevalence rate for children ages one to five in the absence of published studies on this subset.

Some children have both OCD and tic disorders. This comorbidity has long been recognized in the clinical literature, with 20 to 60 percent of tic disorders patients meeting the criteria for OCD.[20] To account for children with one or both disorders, and eliminate double counting, the analysis used the comorbidity rates to determine how many patients with tic disorders do not also have OCD, and then added those patients to the total of all OCD patients. Because a higher rate of comorbidity (the extent to which children with OCD overlap with children with tic disorders) reduces the total number of children at risk of PANDAS/PANS, the low-cost scenario assumed 60 percent of children with tic disorders also had OCD, and the high-cost scenario assumed 20 percent; the mid-cost scenario used the mid-point.

Applying these comorbidity rates to the reported tic disorders prevalence results in population prevalence estimates for patients with tic disorders but not OCD of 0.16 percent in the low-cost scenario (40 percent of 0.4 percent), 0.36 percent in the mid-cost scenario (60 percent of 0.6 percent), and 0.64 percent in the high-cost scenario (80 percent of 0.8 percent). Adding these prevalence rates to the patients with OCD results in combined prevalence rates of 1.16 percent in the low cost scenario, 2.86 percent in the mid-cost scenario, and 4.64 percent in the high-cost scenario. Using the low-end scenario as an example of the combined prevalence calculation, the OCD prevalence of 1.00 percent is added to the prevalence of tic disorders without OCD of 0.16 percent to yield a combined low scenario prevalence of 1.16 percent. Table 1 shows the development of the combined prevalence range of 1.16 to 4.64 percent.

Table 1:
National Prevalence of OCD and/or Tic Disorders (TD)

	TD Prevalence (a)	% of TD with OCD (b)	% of TD w/o OCD (c)=1-(b)	TD Prev. w/o OCD (d)=(c)*(a)	OCD Prevalence (e)	OCD or TD Prevalence (f)=(d)+(e)
Low Scenario	0.40%	60.00%	40.00%	0.16%	1.00%	1.16%
Mid Scenario	0.60%	40.00%	60.00%	0.36%	2.50%	2.86%
High Scenario	0.80%	20.00%	80.00%	0.64%	4.00%	4.64%

4.2. Prevalence of PANDAS/PANS among children with OCD and/or tic disorders

A subset of children with an OCD and/or tic disorders may be diagnosed with PANDAS or PANS. To date there are no published studies on prevalence of the disorders, as they have been fairly recently identified and the diagnostic criteria are subjective and have yet to be codified in the ICD or DSM. The lack of ICD or DSM diagnosis codes for the condition means prevalence cannot be estimated using health care claim data resources, such as the Massachusetts APCD. This analysis bases the estimate of PANDAS/PANS prevalence on an interview[21] with a clinician from the Pediatric Neuropsychiatry and Immunology Program at Massachusetts General Hospital, specializing in treating PANDAS, and a published interview with Susan Swedo, MD, Chief of the Pediatrics and Developmental Neuroscience Branch at the National Institutes of Mental Health (NIMH), who first proposed a link between streptococcal infection in children and some rapid-onset cases of OCD or tic disorders (PANDAS) and more recently recognized PANS.

The interviewed clinician estimated that ten to fifteen percent of children with OCD or tic disorders are diagnosed with PANDAS or PANS during their lifetime. In a 2010 interview with *Scientific American*, Dr. Swedo estimated "that PANDAS kids may make up as much as 25 percent of children diagnosed with OCD and tic disorders, such as Tourette syndrome."[22] These sources suggest a fairly broad range of values for estimated PANDAS/PANS prevalence as a portion of children with an OCD and/or tic disorders. The goal of the analysis is to produce a range of the most likely outcomes, and it therefore assumes that lifetime PANDAS/PANS prevalence is between 13.5 and 21.5 percent of those children.

To estimate the prevalence of PANDAS/PANS among all children, the prevalence of PANDA/PANS among children with an OCD and/or tic disorders was multiplied by the prevalence of OCDs and/or tic disorders among children. Applying the PANDAS/PANS prevalence estimates above (13.5 to 21.5 percent) to the OCD and/or tic disorders prevalence from Table 1 results in a PANDAS/PANS prevalence range of 0.16 percent to 1.0 percent, relative to all children. Multiplying this prevalence rate by 564,423, the estimated total number of children aged 1 to 18 with commercial fully-insured coverage in Massachusetts in 2012, results in a baseline range of 884 to 5,631 children who will at some point develop PANDAS/PANS. These calculations are displayed in Table 2.

Table 2:
Estimated Number of Children Developing PANDAS/PANS in Their Lifetime
Massachusetts Fully-Insured Population

	OCD/TD Prevalence	OCD/TD w/ PANDAS/PANS	Overall Prevalence	Number of Children
Low Scenario	1.16%	13.50%	0.16%	884
Mid Scenario	2.86%	15.00%	0.50%	2,825
High Scenario	4.64%	21.50%	1.00%	5,631

These estimates are converted to the numbers of treatments per year in Section 4.4.

4.3. Treatment types and patterns for PANDAS/PANS

Several treatment types are available for PANDAS/PANS children. Patients are generally treated with cognitive behavior therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs), the standard treatments for OCD and/or tic disorders, as well as the use of prophylactic antibiotics, all of which are generally covered by insurers. Therefore these treatments do not represent an incremental cost of the proposed mandated benefit.

For children for whom these conventional therapies do not work, researchers are currently evaluating several treatments, including tonsillectomy and therapies such as plasma exchange (plasmapheresis) and intravenous immunoglobulin (IVIG) aimed at modifying a patient's immune response.[23,24] There is a broad range in cost for these services, which are considered experimental in the treatment of PANDAS/PANS and are therefore generally not covered by insurers; the cost to insurers of covering these services represents the incremental cost of H.B. 984, if enacted. As a result, this analysis depends upon an estimate of how many children with PANDAS/PANS receive each type of service.

The estimated distribution of the incremental treatment types utilized by the PANDAS/PANS population was developed based upon the interview with the aforementioned Massachusetts clinician who specializes in the treatment of PANDAS.[25] These treatments are further described below:

- Plasmapheresis: Plasmapheresis (plasma exchange), which requires at least a two-day stay in an intensive care unit, is performed for children with PANDAS/PANS by only one clinician in the country, based in Washington, D.C. (and not interviewed or otherwise cited in this review). In a two-year period from 2013 through 2014, only one patient, among approximately two hundred patients seen by the interviewed Massachusetts clinician, was referred to and received plasmapheresis treatment. The PANDAS Physician Network and the NIMH recommend plasmapheresis only for severely to extremely ill patients.[26] However, the American Society for Apheresis recently stated that plasmapheresis should be used as a first-line treatment for PANDAS, indicating its use may increase in the future.[27,28] This analysis assumes 0.3 to 1.0 percent of children will undergo this procedure, and assumes these children will also be treated with prophylactic antibiotics.
- IVIG: IVIG has been proven safe in children for a variety of autoimmune orders, though it can cause serious side effects such as painful headaches. However, its effectiveness for PANDAS/PANS is still being studied and no guidelines have yet been released. The PANDAS Physicians Network recommends its use for moderate to severe illness levels, and the NIMH cautions physicians to balance the risks of the procedure with its potential patient benefits.[29] The Pediatric Neuropsychiatry and Immunology Program at Massachusetts General Hospital convenes a review panel of psychiatry, immunology, and infectious disease specialists to determine which children receive this treatment. Children who are candidates must have severe symptoms despite treatment with SSRIs and/or CBT. The interviewed clinical expert[30] estimated 10 percent of his patients

receive IVIG; this analysis assumes between 10 and 20 percent of children will receive this treatment. Further, this analysis assumes these children will also be treated with prophylactic antibiotics.

- Tonsillectomy: The interviewed clinical expert[31] estimated approximately 10 percent of children with PANDAS/PANS undergo tonsillectomy. A new study published in January 2015 that examined the role of tonsillectomy in the treatment of PANDAS concluded that the specific group of patients in the study "whose neuropsychiatric symptoms did not respond sufficiently to antibiotics may have gained benefit from tonsillectomy."[32] Use of this treatment is new and is expected to increase. However, as tonsillectomy is a standard and accepted treatment for other established pediatric conditions, it is likely that this treatment is currently covered in some cases and in those cases will not represent incremental cost due to this mandate. This analysis therefore assumed a range of incremental tonsillectomies of between 2.5 percent to 7.5 percent of children with PANDAS/PANS.

Table 3 summarizes the estimated distribution of incremental treatment types that will be utilized for children with PANDAS/PANS. The percentages total less than 100 percent because most children will be adequately treated with CBT, SSRIs, prophylactic antibiotics, and/or tonsillectomies (as currently utilized).

Table 3:
Expected Treatment Distribution for PANDAS/PANS

	Plasmapheresis	IVIG	Incremental Tonsillectomy
Low Scenario	0.3%	10.0%	2.5%
Mid Scenario	0.5%	15.0%	5.0%
High Scenario	1.0%	20.0%	7.5%

4.4. Number of treatments per year

Calculating a baseline incremental cost required estimating the number of treatments in a single year. Once onset of PANDAS/PANS occurs, treatment can occur in one or more years depending upon the type. CBT, SSRIs, and prophylactic antibiotics are typically tried first, followed by other treatments like IVIG, plasmapheresis, or tonsillectomies if warranted.

A single infusion of IVIG treatment is used unless a child relapses. A recent journal article on IVIG treatment results for children with PANDAS[33] stated that approximately 50 percent of patients required a second IVIG treatment. This analysis assumed patients receiving IVIG will receive 1.5 IVIG treatments on average, and made a similar assumption for plasmapheresis. Tonsillectomies are a one-time only treatment.

To calculate the annual number of treatments, Compass began by determining the number of children receiving each treatment in their lifetime by multiplying the treatment distribution from Table 3 by the number of children experiencing PANDAS/PANS from Table 2. The resulting

number of users is then multiplied by the estimated number of lifetime treatments per user described above, yielding the total treatments by type. The annual number of treatments was calculated by dividing the total lifetime estimate of PANDAS/PANS treatments by 18. Given the relatively uniform distribution of children by age, the age of onset does not have a significant impact on the number of treatments each year. Table 4 shows the estimated total annual number of treatments for the entire Massachusetts fully insured population.

Table 4:
Estimated Annual Number of Treatments by Treatment Type
Massachusetts Fully-Insured Population

	Plasmapheresis	IVIG	Tonsillectomy
Low Scenario	0.2	7.4	1.2
Mid Scenario	1.2	35.3	7.8
High Scenario	4.7	93.8	23.5

4.5. Cost per treatment

Treatment for PANDAS/PANS, per se, is not currently covered by any of the ten largest carriers in Massachusetts. However, claim data are available in the APCD for each of the above forms of treatment because each is used to treat other covered conditions. Compass calculated annual costs to treat a child with each of the forms of treatment using 2012 claims from the APCD.

- Plasmapheresis is typically performed only once to treat PANDAS/PANS, however children are sometimes treated again if a relapse occurs. Compass calculated average costs for procedure codes for all hospital and physician services comprising a "typical" single episode of plasmapheresis, resulting in an average cost of $17,580.
- For IVIG therapy, children with PANDAS/PANS are typically treated with a single infusion and sometimes treated again if a relapse occurs. Compass calculated an average paid cost per gram of IVIG infusions of $124.31 using 2012 APCD claim data. Total infusion amounts are based upon a child's weight; children are treated with 2 grams of IVIG per kilogram. Compass calculated a weighted average body weight of a PANDAS/PANS patient of 24.5 kilograms by multiplying, for each single year of age, the proportion of children that age by the average weight in pounds per child that age,[34] and then summing across all ages and converting the result to kilograms (at 2.2 pounds per kilogram). At 2 grams of IVIG per kilogram, this implies an average IVIG infusion of 49 grams which, multiplied by the $124.31 per gram cost, results in an average cost per infusion of $6,103. Average physician and facility costs associated with IVIG were measured using the APCD and added to the infusion cost, resulting in a total cost of $7,059 per treatment.
- Tonsillectomies are also used to treat PANDAS/PANS. Procedure codes for tonsillectomies were identified and a cost of $3,351 including all hospital and professional services for a "typical" case was measured using the APCD.

Table 5 displays the estimated cost of each of the treatment types.

Table 5:
Estimated Treatment Cost

	Plasmapheresis	IVIG	Tonsillectomy
Cost per treatment	$17,580	$7,050	$3,351

4.6. Incremental cost calculation

Multiplying the estimated number of treatments by type per year for PANDAS/PANS (from Table 4) by the average treatment cost (from Table 5) and summing across treatment types, yields the incremental claim cost of the proposed mandate. This cost was then divided by the total fully-insured commercial members (member months) in the 2012 base data, yielding the incremental per-member per-month (PMPM) cost. Results are displayed in Table 6.

Table 6:
Estimate of Increase in Carrier 2012 Claim Cost

Low Scenario	$0.002
Mid Scenario	$0.010
High Scenario	$0.027

4.7. Carrier retention and increase in premium

Assuming an average retention rate of 9.7 percent based on CHIA's analysis of administrative costs and profit in Massachusetts, the increase in medical expense was adjusted upward to approximate the total impact on premiums. Table 7 shows the result.

Table 7:
Estimate of Increase in Carrier 2012 Premium Expense

Low Scenario	$0.002
Mid Scenario	$0.011
High Scenario	$0.030

4.8. Projected fully-insured population in Massachusetts

Table 8 shows the fully-insured population in Massachusetts ages 0 to 64 projected for the next five years. Appendix A describes the sources of these values.

Table 8:
Projected Fully-Insured Population in Massachusetts, Ages 0-64

Year	Total (0-64)
2016	2,329,040
2017	2,304,658
2018	2,279,367
2019	2,253,405
2020	2,226,328

4.9. Projection

The incremental spending was projected for the period January 1, 2016 to December 31, 2020 using an annual health care expenditure inflation rate from a study from the Centers for Medicare and Medicaid Services (CMS);[35] annual cost increases are in the range of 2.5 to 6.0 percent and average 4.6 percent. The trended incremental PMPM premiums were multiplied by the member months displayed in Table 8 to calculate total incremental costs. The results of these calculations are presented in the next section.

5. Results

The results of the estimated impact of the mandate are outlined below. The analysis includes development of a best estimate "middle-level" scenario, as well as a low-level scenario using assumptions that produced a lower estimate, and a high-level scenario using more conservative assumptions that produced a higher estimated impact.

5.1. Five-year estimated impact

For each year in the five-year analysis period, Table 9 displays the projected net impact of the mandate on medical expense and premiums using a projection of Massachusetts fully-insured membership. Note that the relevant provisions of H.B. 984 are assumed to be effective January 1, 2016.[36]

The low scenario impact is very small at $77,000 per year on average, and is due to the lower prevalence rate and utilization of incremental treatment by those children with PANDAS/PANS. The high scenario has average cost of $1.1 million per year, and reflects an estimate that a higher portion (1.0 percent) of the population of children will get PANDAS/PANS, in addition to assuming higher utilization of treatment. The mid-scenario has average annual costs of $387,000, or an average of 0.003 percent of premium.

Finally, the impact of the proposed law on any one individual, employer-group, or carrier may vary from the overall results depending on the current level of benefits each receives or provides, and on how the benefits will change under the mandate.

Table 9: Summary Results

	2016	2017	2018	2019	2020	Weighted Average	5 Yr Total
Members (000s)	2,329	2,305	2,279	2,253	2,226		
Medical Expense Low ($000s)	$46	$67	$69	$72	$75	$70	$329
Medical Expense Mid ($000s)	$230	$335	$345	$359	$372	$349	$1,642
Medical Expense High ($000s)	$641	$931	$959	$998	$1,035	$971	$4,564
Premium Low ($000s)	$51	$74	$77	$80	$83	$77	$364
Premium Mid ($000s)	$255	$371	$382	$398	$412	$387	$1,819
Premium High ($000s)	$710	$1,031	$1,063	$1,105	$1,147	$1,076	$5,056
PMPM Premium Low	$0.003	$0.003	$0.003	$0.003	$0.003	$0.003	$0.003
PMPM Premium Mid	$0.013	$0.013	$0.014	$0.015	$0.015	$0.014	$0.014
PMPM Premium High	$0.036	$0.037	$0.039	$0.041	$0.043	$0.039	$0.039
Estimated Monthly Premium	$473	$487	$501	$515	$530	$487	$487
Premium % Rise Low	0.001%	0.001%	0.001%	0.001%	0.001%	0.001%	0.001%
Premium % Rise Mid	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%
Premium % Rise High	0.008%	0.008%	0.008%	0.008%	0.008%	0.008%	0.008%

5.2. Impact on the GIC

The proposed mandate is assumed to apply to both fully-insured and self-insured plans operated for state and local employees by the Group Insurance Commission (GIC), with an effective date for all GIC policies on July 1, 2016.

Because the benefit offerings of GIC plans are similar to most other commercial plans in Massachusetts, and likewise do not currently cover treatment for PANDAS/PANS similarly to other carriers, the estimated PMPM effect of the proposed mandate on GIC coverage is not expected to differ from that calculated for the other fully-insured plans in Massachusetts. To estimate the medical expense separately for the GIC, the PMPM medical expense for the general fully-insured population was applied to the GIC membership starting in July of 2016.

Table 10 breaks out the GIC-only fully-insured membership and the GIC self-insured membership and the corresponding incremental medical expense and premium. Note that the total medical expense and premium values for the general fully-insured membership displayed in Table 9 also include the GIC fully-insured membership. Finally, the proposed mandate is assumed to require the GIC to implement the provisions on July 1, 2016; therefore, the results in 2016 are approximately one-half of an annual value.

Table 10:
GIC Self-Insured Summary Results

	2016	2017	2018	2019	2020	Weighted Average	5 Yr Total
GIC Fully-Insured							
Members (000s)	59	59	59	59	59		
Medical Expense Low ($000s)	$1	$2	$2	$2	$2	$2	$8
Medical Expense Mid ($000s)	$4	$9	$9	$9	$10	$9	$41
Medical Expense High ($000s)	$12	$24	$25	$26	$27	$25	$114
Premium Low ($000s)	$1	$2	$2	$2	$2	$2	$9
Premium Mid ($000s)	$5	$10	$10	$10	$11	$10	$45
Premium High ($000s)	$13	$26	$28	$29	$30	$28	$126
GIC Self-Insured							
Members (000s)	263	263	263	262	262		
Medical Expense Low ($000s)	$4	$8	$8	$8	$9	$8	$36
Medical Expense Mid ($000s)	$18	$38	$40	$42	$44	$40	$182
Medical Expense High ($000s)	$51	$106	$111	$116	$122	$112	$506

Appendix A: Membership Affected by the Proposed Mandate

Membership potentially affected by a proposed mandate may include Massachusetts residents with fully-insured employer-sponsored health insurance (including through the GIC), non-residents with fully-insured employer-sponsored insurance issued in Massachusetts, Massachusetts residents with individual (direct) health insurance coverage, and, in some cases, lives covered by GIC self-insured coverage. Membership projections for 2016 to 2020 are derived from the following sources.

Total Massachusetts population estimates for 2012, 2013, and 2014 from U. S. Census Bureau data[37] form the base for the projections. Distributions by gender and age, also from the Census Bureau,[38] were applied to these totals. Projected growth rates for each gender/age category were estimated from Census Bureau population projections to 2030.[39] The resulting growth rates were then applied to the base amounts to project the total Massachusetts population for 2016 to 2020.

The number of Massachusetts residents with employer-sponsored or individual (direct) health insurance coverage was estimated using Census Bureau data on health insurance coverage status and type of coverage[40] applied to the population projections.

To estimate the number of Massachusetts residents with fully-insured employer-sponsored coverage, projected estimates of the percentage of employer-based coverage that is fully-insured were developed using historical data from the Medical Expenditure Panel Survey Insurance Component Tables.[41]

To estimate the number of non-residents covered by a Massachusetts policy – typically cases in which a non-resident works for a Massachusetts employer offering employer-sponsored coverage – the number of lives with fully-insured employer-sponsored coverage was increased by the ratio of the total number of individual tax returns filed in Massachusetts by residents[42] and non-residents[43] to the total number of individual tax returns filed in Massachusetts by residents.

The number of residents with individual (direct) coverage was adjusted further to subtract the estimated number of people previously covered by Commonwealth Care who moved into MassHealth due to expanded Medicaid eligibility under the Affordable Care Act.[44]

Projections for the GIC self-insured lives were developed using GIC base data for 2012,[45] 2013,[46] and 2014[47] and the same projected growth rates from the Census Bureau that were used for the Massachusetts population. Calculations of GIC self-insured lives used breakdowns of the population by gender and age based on Census Bureau distributions.

Endnotes

[1] The 188th General Court of the Commonwealth of Massachusetts, House Bill 984, "An Act relative to treatment for PANDAS/PANS". Accessed 6 February 2015: https://malegislature.gov/Bills/188/House/H984. In the 189th General Court of the Commonwealth of Massachusetts, House Bill 944; accessed 16 March 2015: https://malegislature.gov/Bills/189/House/H944.

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