



# PHILIPPINE SOCIETY OF OTOLARYNGOLOGY - HEAD AND NECK SURGERY

## Clinical Practice Guidelines

Acute Otitis Media in Children  
Cleft Lip Alveolus and Palate  
Allergic Rhinitis in Adults  
Acute Bacterial Rhinosinusitis in Adults  
Chronic Rhinosinusitis in Adults

## Clinical Practice Guidelines Working Group

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## FOREWORD

We take pride in this first of a series of releases of the 2016 PSOHNS clinical practice guidelines. This release includes updated versions of the guidelines on allergic rhinitis, acute bacterial rhinosinusitis and chronic rhinosinusitis in adults. Significantly, there are new guidelines that address acute otitis media in children, and cleft lip alveolus and palate. Starting in 2015, the study groups representing the relevant ENT subspecialties met with the Guideline Committee to select the existing guidelines to update and the topics for the guidelines to be developed. They also adopted a standard guideline reporting format and development process as defined by the Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument. With technical assistance and computing services provided by PSOHNS, members of the subspecialty study groups wrote the initial guideline drafts which were then presented to the institutions with ENT residency training programs and to the regional chapters of PSOHNS. Copies of the CPGs were then sent to the general membership of PSOHNS and relevant external experts for comments. The study groups then revised the drafts accordingly. In 2016, the CPGs underwent peer review.

The previous set of guidelines has been widely used as ‘must reads’ of ENT residents in training and as such were used to evaluate care delivered by residents in training. We hope that the 2016 series will be extensively used to improve patient outcomes by changing professional practice, shaping ENT care policies and driving new research. For these to happen, the guidelines have to be widely discussed and adapted to specific clinical settings.

Guidelines do not implement themselves. Clinical pathways, that is, institution – specific protocols and pre-printed order sets, based on the strongest guideline recommendations, must be developed by multidisciplinary hospital groups. Pathways have been proven to effectively translate guideline recommendations into process and outcome improvements. We, otolaryngologists, can demonstrate leadership by heading these pathway groups and championing pathway implementation.

Guidelines are not cast in stone. They are living, breathing documents which should be critically appraised, just like any form of research, for their validity and applicability. They have expiry dates that should trigger automatic re-evaluation and revision. They are like cars that depreciate once they are released from their makers. Thus, we should be alert to new evidence that may modify or reverse their recommendations.

Guidelines do not dictate care, only guide it. Guidelines should not be used to unreasonably standardize care. As doctors we are required to bend care to respond to unique patients’ needs, not blindly adhere to guidelines. Rather we can use guidelines during audits and peer reviews to debate, discuss and learn from our colleagues’ care decisions and the consequent outcomes of such care. This invites healthy professional competition and benchmarking. Our patients should ultimately benefit from sensible guideline adoption.

# Acute Otitis Media in Children

Philippine Academy of Neurotology, Otology and Related Sciences

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### SCOPE OF THE PRACTICE GUIDELINES

These clinical practice guidelines are for the use of the Philippine Society of Otolaryngology-Head and Neck Surgery. It covers the diagnosis and management of acute otitis media in children 2 months to 12 years of age.<sup>1,2</sup>

### OBJECTIVES

The objectives of the guideline are (1) to emphasize the requisites for the diagnosis of acute otitis media in children and (2) to describe treatment options based on current evidence.<sup>3</sup>

### LITERATURE SEARCH

The National Guideline Clearing House, Society for Middle Ear Disease Organization and Cochrane Ear, Nose and Throat Disorders Group of the National Institute for Health Research were searched for guidelines on acute otitis media. Additional Search Strategy included electronic databases (Cochrane Database, Medline, CINAHL, Pubmed Database, ScienceDirect, DOAJ, Biomed Central), local libraries, including attempts of searching for unpublished literature. Electronic database were searched using the keywords *otitis media* to include *acute otitis media* limited to the English language. The search yielded 19,653 articles.

Forty five articles were chosen for review and were divided as follows:

Meta-analysis/Systematic Review	10
Randomized Controlled Trial	7
Descriptive/Cohort	12
Clinical Practice Guidelines	16

The level of recommendation and evidence for therapeutic studies from the American Society of Plastic Surgeons Evidence-based Clinical Practice Guidelines were used in the grading of recommendations for this guideline.

Table 1. Levels of Recommendation

Grade	Descriptor	Qualifying Evidence	Implications for Practice
A	Strong recommendation	Level I evidence or consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role
D	Option	Level V evidence: little or no systematic empirical evidence	Clinicians should consider all options in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role

From the American Society of Plastic Surgeons. Evidence-based clinical practice guidelines.

**Table 2.** Level of Evidence for Therapeutic Studies

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence intervals)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual Cohort study (including low quality RCT, e.g. <80% follow-up)
2C	“Outcomes” research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual Case-control study
4	Case series (and poor quality cohort and case-control study)
5	Expert opinion without explicit critical appraisal or based on physiology bench research or “first principles”

From the Centre for Evidence-Based Medicine

**DEFINITION**

**Acute otitis media (AOM)** is defined as an acute middle ear inflammation. It is characterized by signs and symptoms of middle ear inflammation with or without the presence of effusion of less than 3 weeks duration<sup>4</sup>.

**ETIOLOGY**

AOM can be due to multiple multiple organisms such as viruses and bacteria. The most common cultures AOM bacteria are *Streptococcus pneumoniae*, non-typable *Hemophilus influenzae* and *Moraxella catarrhalis*. Among cases of AOM the most commonly isolated bacterial pathogens are *S.pneumoniae* in 25-50%, *H.influenza* in 15-30% and *M.catarrhalis* in 3-20%. The common AOM viruses in children are respiratory syncytial virus, rhinovirus, coronavirus, parainfluenza, adenovirus and enterovirus. There is still controversy whether all these viruses are pathogens that cause AOM, but it has been identified that adenovirus poses the greatest risk of causing AOM after a bout of upper respiratory tract infectin. Co-infection with a viral cause of AOM has been a suspected reason for failure of antibiotic therapy<sup>4</sup>.

**NATURAL HISTORY OF ACUTE OTITIS MEDIA<sup>4,5</sup>.**

AOM may be clinically seen in any of the following natural occurring stages:

**1. Stage of Hyperemia/ Retraction**

This is the onset of disease, which is characterized by a generalized

hyperemia of the mucoperiosteum. Symptoms will include mild earache, ear fullness and fever. An erythematous and markedly retracted eardrum is seen upon otoscopy.

**2. Stage of Exudation**

This stage marks the outpouring of fluid from the dilated permeable capillaries. All symptoms are aggravated especially pain and fever. A red and thickened bulging eardrum with loss of the light reflex is seen on otoscopy.

**3. Stage of Suppuration / Perforation**

During this stage the eardrum ruptures and there is a lot of discharge seen from the middle ear. Fever and pain are relieved but hearing loss seems to have worsened.

**4. Stage of Coalescence and Surgical Mastoiditis**

This stage is marked by a milder recurrence of pain, mastoid tenderness and fever. Mastoid tenderness and sagging of the posterosuperior wall are revealed upon further evaluation of the patient.

**5. Stage of Complication**

This stage marks the extension of the infection beyond the middle ear.

**6. Stage of Resolution**

This stage may occur at any stage of the disease.

**PREVALENCE AND EPIDEMIOLOGY**

AOM can affect any age group, although epidemiologic studies report that it is more common among children younger than 3 years of age. Two thirds of these children are expected to have one episode of AOM during childhood and one third of them will have more than three episodes before they reach the age of 2. Thus age is an important factor in the incidence of AOM.

A wide range of AOM incidence rates can be found in different countries. In the Asia-Pacific region, incidence ranges from 0.69% among Thai school children aged 7-9 years old to 33% among Australian aboriginal children aged 6 to 30 months. Reports from both Europe and the US, show that 62% of children aged less than one year and 83% of those up to the age of three have suffered at least one bout of AOM. In the Philippines, a cross sectional survey of children ages 0 – 12 years old showed an overall prevalence of AOM at 9.6%, with the 0 to 2 year age group having the highest prevalence<sup>4</sup>. By means of extrapolation there were approximately 2,721,676 children that were presumed to have acute otitis media (out of 228,427,779 among the 0-14 age group, based on Philippine Health Statistics done in 2005). According to the 2007 National Statistics Data, around 2% of all antibiotic prescriptions in the Philippines were for the treatment of AOM. The estimated cost of antibiotic treatment for AOM among the pediatric population was estimated to be around 5.7 billion Philippine pesos.<sup>6</sup>

**RISK FACTORS**

Risk factors for AOM are not exactly involved in its pathophysiology, rather their presence may indicate a higher chance of AOM occurrence. These risk factors are divided into non-modifiable host related risk factors (age, sex, race, genetic predisposition) and environment-related modifiable risk factors (exposure to smoke, poor socioeconomic status, congested living conditions, daycare center attendance, previous use of antibiotics, bottle feeding and use of pacifiers)<sup>4,5</sup>

In a systematic review of the risk factors associated with AOM among indigenous people in Australia, it was found that swimming pool use may

also attribute to AOM occurrence. Additional host-related risk factors identified included premature birth, allergies, immunological deficiency, cleft palate defects, craniofacial abnormalities and adenoid hypertrophy. Seasonality as another environmental factor may increase the risk of otitis media.<sup>7</sup> In contrast to most western countries, the Philippines has only two seasons: the rainy season (from June to November) and the dry season (from December to May)<sup>8</sup>.

**RECOMMENDATIONS FOR THE DIAGNOSIS OF ACUTE OTITIS MEDIA**

**1. Diagnosis of acute otitis media is based mainly on clinical parameters. A good clinical history and physical examination, particularly otoscopy and pneumatic otoscopy can obtain criteria that will fulfill the clinical diagnosis of acute otitis media<sup>4</sup>.**

*Grade B Recommendation Level 3A Evidence*

**1.1 Diagnosis of acute otitis media requires**

- 1.1.1 *History of acute (within 3 weeks) onset and*
- 1.1.2 *Signs and symptoms of middle ear inflammation and*
- 1.1.3 *Presence of middle ear effusion*

**1.2 Any of the following otoscopic findings**

- 1.2.1 *Limited or absent mobility of the tympanic membrane<sup>9,4</sup>*  
Best predictor of AOM (high sensitivity 95%, high specificity 85%)<sup>9</sup>
- 1.2.2 *Cloudiness of tympanic membrane<sup>9,4</sup>*  
High sensitivity 74% and high specificity 97%<sup>9</sup>
- 1.2.3 *Bulging of the tympanic membrane<sup>9,4</sup>*  
Low sensitivity 51% and high specificity 97%<sup>9</sup>
- 1.2.4 *Markedly retracted tympanic membrane<sup>9,4</sup>*
- 1.2.5 *Distinct erythema of the tympanic membrane<sup>4</sup>*
- 1.2.6 *Air-fluid level or air bubbles behind the tympanic membrane<sup>9,4</sup>*
- 1.2.7 *Perforation with otorrhea<sup>9</sup>*

**A good clinical history and otoscopic examination of the tympanic membrane is the key to the correct diagnosis of AOM.**

**1.3 Any of the following findings**

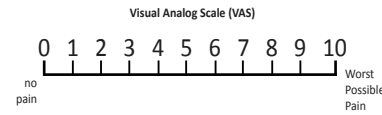
- 1.3.1 *Otalgia*  
Older children with AOM usually present with a history of rapid ear pain. Among young preverbal children tugging, rubbing or holding of the ear may suggest otalgia. Excessive crying and changes in the child's sleep pattern may also suggest otalgia<sup>9</sup>.
- 1.3.2 *Fever*  
Acute occurrence of otalgia, fever and/or otorrhea supports the diagnosis of AOM but is nonspecific as an entity. In relation to the diagnosis of AOM, it has a sensitivity of 54% and a specificity of 82%<sup>10</sup>.

**Mild symptoms** include mild otalgia on the visual analog scale with a duration of less than 48 hours and body temperature of less than 39°C.<sup>9</sup>

**Moderate to Severe symptoms** include otalgia on the visual analog

scale with a duration of at least 48 hours and body temperature of 39°C or more.<sup>9</sup>

**Figure 1. Visual Analog Scale**



**2. Pneumatic otoscopy is recommended as a primary tool in the diagnosis of middle ear effusion.**

*Grade B Recommendation Level 2B Evidence*

An important criteria for AOM diagnosis is the presence of middle ear fluid. In order to identify signs and symptoms of middle ear effusion, confirmation with the use of pneumatic otoscopy is recommended<sup>4</sup>. Pneumatic otoscopy is 70-90% sensitive and specific for determining the presence of middle ear effusion (MEE) when compared to 60-70% accuracy with simple otoscopy<sup>11</sup>. Findings include limited or absent mobility of the tympanic membrane, which is the best predictor of AOM (high sensitivity 95%, high specificity 85%), cloudiness of tympanic membrane with (high sensitivity 74% and high specificity 97%) and bulging of the tympanic membrane (low sensitivity 51% and high specificity 97%)<sup>12</sup>. There can be difficulty in the assessment of the tympanic membrane of infants and young children due to problems with cooperation, the external auditory meatus anatomy and the presence of cerumen. In such cases the diagnosis of AOM cannot be made certain. The use of pneumatic otoscopy in order to confirm the restricted mobility of the tympanic membrane can be helpful but may also present problems when performed among small children<sup>13,14</sup>.

**3. Tympanometry is not routinely recommended in the diagnosis of AOM.**

*Grade C Recommendation Level 2B Evidence*

The sensitivity and specificity of tympanometry, using pneumatic otoscopy as a gold standard, has been assessed. The presence of a type A or normal tympanogram does not completely rule out the presence of air-fluid levels and effusion in the middle ear. Only when performed together with normal otoscopy can it be predictive of the lack of middle ear fluid. A type B or flat tympanogram should be confirmed by means of repeated measurements and by the correlation of tympanometry with pneumatic otoscopy<sup>15</sup>.

A particular disadvantage of tympanometry is that it requires a good seal of the external auditory canal. A tympanogram cannot be obtained in children who often move or cry because an adequate seal cannot be obtained<sup>16</sup>.

**4. Tympanocentesis is not routinely recommended in the diagnosis of acute otitis media.**

*Grade C Recommendation Level 2B Evidence*

Tympanocentesis is the gold standard for bacteriologic diagnosis but it is not usually indicated in the diagnosis of acute otitis media<sup>4</sup>.

**RECOMMENDATIONS FOR THE TREATMENT OF ACUTE OTITIS MEDIA**

**1. Pain relief is an important part of effective AOM management. Treatment in order to address otalgia is recommended.**

*Grade B Recommendation Level 3A Evidence*

Most of the articles that were reviewed and the consensus taken from different groups agreed that pain associated with acute illness should be addressed<sup>17</sup>. Treatment options should be based on the severity of illness with incorporation of the preference of the parent/caregiver and the patient. Consideration of benefits and risks should be done whenever possible<sup>18</sup>. Pain should be addressed during the first 24 hours upon diagnosis. Paracetamol (10-15 mg/Kg/dose) and Ibuprofen (5-10mg/Kg/dose) are the mainstay of treatment that can provide analgesia for mild to moderate pain<sup>19</sup>.

The use of topical anesthetics is currently not recommended because there was a paucity of evidence with regards to its benefits among patients who concurrently took oral analgesics when they were compared to patients who concurrently took placebo medications<sup>19</sup>.

**2. Initial observation is an option among children two years and older with mild symptoms and among infants 6 to 23 months old with unilateral mild AOM.**

*Grade B Recommendation Level 2A Evidence*

Initial observation for AOM refers to deferment of antibacterial treatment for the first 48 to 72 hours while providing symptomatic relief.<sup>19</sup> Observation must be a joint decision between the clinician and the parents or caregiver. In such cases, a system for close follow-up and a means of beginning antibiotics must be in place if symptoms worsen or no improvement is seen within the initial 48 to 72 hours. Safety net antibiotic prescriptions (SNAP) can be given at the initial visit with a specific instruction that it will be used only when the condition of the child persists or worsens after 48 to 72 hours.<sup>20</sup> SNAP prescriptions should be dated so as to prevent the inappropriate use of antibiotics<sup>15</sup>.

Parents or caregivers should be educated about the self-limiting nature of most cases of AOM, the importance of pain relief early in the course, and the possible side effects of antibacterials (i.e. hypersensitivity, vomiting, diarrhea and diaper rash)<sup>9</sup>.

- 3. Initial antibiotic therapy should be prescribed among the following:**
- a. Children 6 months and older with severe signs or symptoms of unilateral or bilateral disease and,
  - b. Children less than 2 years old with bilateral disease without severe signs or symptoms

*Grade B Recommendation Level 2A Evidence*

Initial antibiotic therapy is defined as treatment of AOM with antibiotics prescribed upon diagnosis, which has the intent of starting antibiotic therapy as soon as possible. A recent systematic review that compared the effectiveness of antibiotic and placebo in the initial treatment of uncomplicated AOM showed that antibiotic use provided a marginal benefit with regards to pain relief during the early stages of the disease.<sup>21</sup> Some experts believe that children aged less than two years and children with bilateral disease or with otorrhea need antimicrobials

for their initial AOM treatment.<sup>5</sup> The Europeans and the Americans may differ in the institution of symptomatic relief as initial treatment for AOM but they both agree that antimicrobials should immediately be given to children of ages less than 6 months, have fever greater than 39°C or have severe otalgia. These three indicators have been associated with a greater likelihood of treatment failure and serious infection.<sup>3</sup> On the other hand, several studies have considered children with an age of less than 2 years to be an indication for immediate antibiotic therapy regardless of any other associated risk factor.<sup>22,23</sup>

**Table 3.** Indications for antibacterial treatment versus observation in children with uncomplicated AOM<sup>24</sup>

Age	Moderate or Severe AOM	Mild AOM
< 6 months	Antibacterial Treatment	Antibacterial Treatment
6 months to 2 years	Antibacterial Treatment	Antibacterial treatment in bilateral AOM Observation in unilateral AOM
≥ 2 years	Antibacterial Treatment	Observation

**4. High dose amoxicillin is recommended as the first-line treatment among most patients with mild AOM.**

*Grade A Strong Recommendation Level 1A Evidence*

Amoxicillin is recommended as first line therapy based on its favorable pharmacologic profile against drug-resistant pneumococci, its proven efficacy, safety profile, narrow spectrum of activity and low cost.<sup>9</sup>

Amoxicillin (80-90 mg/Kg/day in 2 divided doses) is effective in inhibiting most non-susceptible strains of pneumococci and to achieve adequate concentration of the drug in the middle ear fluid.<sup>9,22</sup> Amoxicillin, given in high-doses, is able to maintain a minimal inhibitory concentration (MIC) of antibiotic in the middle ear, exceeding the MICs of intermediate and high-level penicillin-resistant *S. pneumoniae*.<sup>25,26</sup> In 2014, Philippine data reported that resistance of *Streptococcus pneumoniae* to Penicillin was 7% - 10.3% (n=257; 95% CI: 5.9-13.4) while there was a Penicillin resistance of 6.6% to 13.4% for *Haemophilus influenzae*.<sup>27</sup> Resistance to co-trimoxazole was reported to be between 17% to 23% for *Streptococcus pneumoniae* and 22% to 43% for *Haemophilus influenzae* from 2008 to 2014.<sup>27</sup>

**5. An antibiotic with β-lactamase coverage is recommended as a first line treatment for severe AOM or when a child's symptoms worsen or fail to respond to initial amoxicillin treatment. (Figure 2)**

*Grade B Recommendation Level 2B Evidence*

Severe AOM suggests a more severe disease or the presence of resistant strains necessitating Amoxicillin with clavulanic acid (90mg/Kg/day amoxicillin plus 6.4mg/Kg/day of clavulanic acid) as initial therapy.<sup>4</sup>

**6. If the patient is allergic to amoxicillin, alternative drugs should be considered.**

*Grade C Recommendation Level 2B Evidence*

Depending on the type of allergic reaction observed, several antibiotics can be recommended.

**Table 4.** Alternative drugs to amoxicillin for allergic patients.<sup>5</sup>

Type I Hypersensitivity Reaction*	Non-Type I Hypersensitivity Reaction**
Azithromycin (10 mg/Kg/day once daily on Day1, followed by 5 mg/Kg/day on day 2-5)	***Cefdinir (14 mg/Kg/day in 1 or 2 doses)
Clarithromycin (15 mg/Kg/day in 2 divided doses for 10 days)	Cefpodoxime (10 mg/Kg/day once daily)
Erythromycin (30-50 mg/Kg/day in 3 divided doses)	Cefuroxime (30 mg/Kg/day in 2 divided doses)
Sulfamethoxazole-Trimethoprim (6-12 mg/Kg/day trimethoprim in 2 divided doses)	Cefixime (8mg/Kg/day once a day or in 2 divided doses)

\*Type I hypersensitivity is immediate or anaphylactic hypersensitivity. The reaction takes 15-30 minutes from the time of exposure to the antigen.

\*\*Non-Type I hypersensitivity is not an immediate reaction and may involve other mechanisms of allergy.

\*\*\* Not available in Philippines (Philippine National Drug Formulary)

Clindamycin (30 mg/Kg/day TID) can be used for patients who are allergic to penicillin and are penicillin-resistant *S pneumonia* suspects. A single dose of parenteral ceftriaxone (50 mg/kg) has been shown to be equivalent to 10 days of amoxicillin and has been known to be effective for patients who cannot tolerate the oral form of antibiotic treatment<sup>4</sup>. A five-day single-dose azithromycin regimen was shown to provide clinical results parallel to 10 days worth of amoxicillin-clavulanic acid as well<sup>4</sup>. Cefixime has excellent activity against  $\beta$ - lactamase-producing *H. influenzae* and *M. catarrhalis* but has significantly weaker activity against *S. pneumoniae* than amoxicillin. Therefore, cefixime may be a good choice for AOM unresponsive to agents with high activity against *S. pneumoniae*, as these cases of AOM are likely attributed to *H. influenzae* or *M. catarrhalis*.<sup>28</sup> In severe cases of AOM that do not respond to antibacterial therapy, a referral to a specialist may be warranted for tympanocentesis. The tympanocentesis may lead to a definitive identification of the involved pathogen and may further provide a better evaluation of the disease<sup>3</sup>.

**7. Duration of antibiotic treatment should depend on the age of the patient and the severity of the disease.**

*Grade A Strong Recommendation Level 1A Evidence*

Antimicrobial treatment for 10-14 days continues to be the current clinical practice for AOM.<sup>4</sup> A standard 10-day course is favored over

shorter courses in children younger than 2 years. In mild to moderate cases, 7 days of antibiotics is preferred for children 2 to 5 years of age and a 5 to 7 day course for children 6 years and older.<sup>9</sup>

In a Cochrane review that compared short and long course antibiotics for AOM, children in the former group had a higher treatment failure rate when they were compared to children who received longer courses of antibiotics (OR: 1.44; 95% CI: 1.21–1.71)<sup>18</sup>. In another systematic review, it was found that short-course azithromycin (3-5 days), had a low risk of treatment failure<sup>29</sup>.

For time-dependent antibacterial agents such as penicillins (amoxicillin) and cephalosporins, drug concentrations must be maintained above the minimum inhibitory concentration for at least 40% of the dosing interval in order to maintain its efficacy. The efficacy of these drugs increase along with their concentrations. Therefore the bactericidal activity of these antibacterials are dependent on their length of exposure to the pathogen. This principle may explain a risk of treatment failure when amoxicillin is given for a short course<sup>29</sup>.

**8. Clinicians must reassess the patient if the symptoms worsen or fail to respond to the initial management options within the first 48-72 hours in order to confirm the diagnosis of AOM, to determine the existence of possible complications and to exclude other causes of the illness.**

**8.1. If the patient was initially managed with observation, management options include the initiation of antibacterial therapy.**

**8.2. If the patient was initially managed with an antibacterial agent (s), management options include 1) change of the antibacterial agent(s); or 2) tympanocentesis or myringotomy in addition to modification of the antibacterial therapy.**

*Grade C Recommendation Level 3A Evidence*

Within 24 hours of antibiotic therapy, the patient’s condition is expected to stabilize. Pain relief is a useful indicator of treatment response.<sup>4</sup> The time course for clinical response should be within 48-72 hours. Criteria for response include the following: 1) defervescence within 48-72 hours, 2) decrease in irritability and 3) normalization of sleep/eating patterns.

If AOM is confirmed in a patient initially managed with observation but has not been noted to clinically improve, the clinician should begin antibacterial therapy. A patient who was initially given amoxicillin may be shifted to high dose amoxicillin with clavulanic acid (90 mg/Kg/day + 6.4 mg/Kg/day). A 3-day course of once daily dosing of Ceftriaxone (50mg/Kg/day IV/IM) may be given to patients with vomiting.<sup>3</sup> In a local study, a single 50 mg/Kg IM dose of Ceftriaxone was shown to be effective for the treatment of uncomplicated AOM and did not show any significant side-effects.<sup>30</sup>

Tympanocentesis or myringotomy may provide immediate pain relief. The procedure may also establish a microbiological analysis of the aspirate in order to isolate the pathogens involved and affirm their antibiotic sensitivities especially among AOM cases that have failed to respond to various antibiotic regimens<sup>9,18,25</sup>. Grevers mentioned that tympanocentesis is only indicated for treatment of complications of AOM, treatment failures and in conditions wherein imminent tympanic membrane perforations cannot be avoided<sup>31</sup>.



**Table 5.** Antibiotic treatment after 48-72h of failure of Initial Antibiotic Treatment<sup>9</sup>

First-Line treatment	Alternative Treatment
Amoxicillin-Clavulanate (90mg/Kg/day amoxicillin with 6.4 mg/Kg/day clavulanate in 2 divided doses)	Ceftriaxone, 3 days Clindamycin (30-40 mg/Kg/day in 3 divided doses) w/ or w/o third-generation cephalosporin
	Clindamycin (30-40 mg/Kg/day in 3 divided doses) plus third generation cephalosporin
Ceftriaxone (50 mg/Kg IM or IV once a day for 3 days)	Tympanocentesis or Myringotomy
	Specialist consultation

**9. The use of antihistamine and/or decongestant therapy is not recommended for the treatment of acute otitis media.**

*Grade A Strong Recommendation Level 1B Evidence*

Antihistamine/decongestant therapy is not recommended for the management of AOM. Upon review of the Cochrane database, studies that examined the efficacy of antihistamines or decongestants upon identification of acute signs or symptoms of AOM, found no significant differences between treatment groups. The use of antihistamines and/or decongestants did not appear justified in the treatment of AOM and is therefore not recommended given their known side effects<sup>18</sup>. However, it was recognized that these agents may be used for concomitant illnesses such as allergies.<sup>4</sup>

**10. Clinicians should recommend pneumococcal conjugate vaccine to all children.**

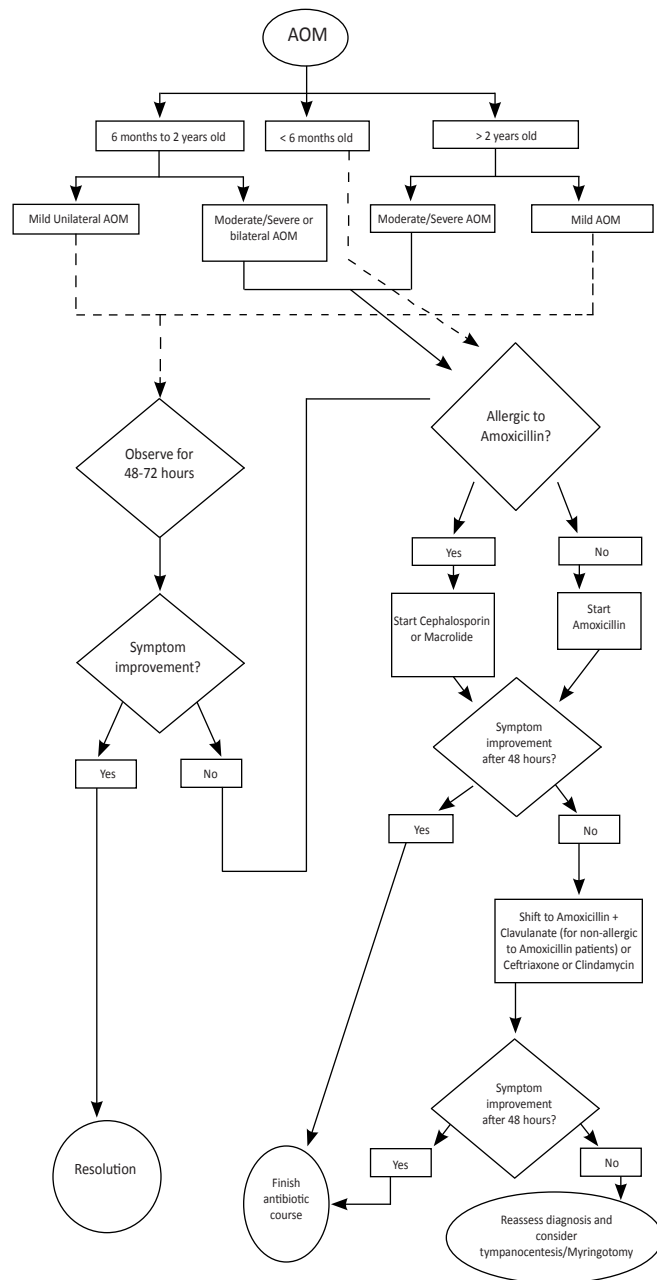
*Grade B Recommendation Level 2A Evidence*

In a recent systematic review on the effects of PCV vaccination in AOM prevention, the use of PCV-7 showed modest beneficial effects among healthy infants but it was unable to reduce overall AOM episodes. Furthermore, the administration of PCV 7 among older children with a history of AOM had no beneficial effect on preventing future episodes of AOM. On the other hand, the use of PCV-11 showed overall reduction in all causes of AOM<sup>32</sup>.

The incorporation of PCV-7 in routine childhood immunization programs in the US proved to be cost effective. An Asian study done in Singapore showed the cost effectiveness of PCV-7 on vaccinated infants when herd immunity was present. Overall, pneumococcal conjugate vaccines have proven to be safe and immunogenic among young children<sup>4</sup>.

In the Philippines, a cohort study done among children 2 to 6 months old showed no difference in the development of AOM in children whether they were given PCV or not. However, the relative risk data derived from this study showed that the vaccine was beneficial in preventing AOM<sup>33</sup>. Further studies are still needed in order to determine the effects of widespread implementation of PCV on AOM, the effects of other serotypes of PCV on AOM, and the risks of complications that PCV vaccine may impose in the general population. However, the overall reduction of AOM cases that may be brought about by the use of PCV-11 may prove to be more beneficial and cost effective in the future.

**Figure 2.** Algorithm for Treatment of AOM in children



**11. Clinicians may recommend annual influenza vaccine to all children.**

*Grade C Recommendation Level 2B Evidence*

Upper respiratory tract infections usually caused by viruses may result in AOM particularly in young children. The administration of influenza vaccine demonstrated efficacy in the prevention of AOM by 30% to 55%.<sup>9</sup> In another study done among children aged 7-50 months, it was found that influenza vaccine had an 83% efficacy rate against influenza-associated AOM and a 36% efficacy against all-cause AOM.<sup>34</sup> In the US, Influenza vaccine is now recommended for all children 6 months of age and older.<sup>9</sup> Influenza vaccine has to be encouraged because it may be useful in the prevention of first AOM episodes<sup>35</sup>. However, a recent Cochrane review revealed that the influenza vaccine had no effect on drug prescription rates, the prevention of AOM, as well as the consequences of vaccination and the socioeconomic impact of the influenza vaccine<sup>36</sup>.

**12. Clinicians should encourage exclusive breastfeeding for at least 6 months**

*Grade B Recommendation Level 3A Evidence*

Breast milk contains lactoferrin, secretory IgA and antibodies. It stimulates the infant's immune response and interferes with bacterial attachment to the nasopharynx<sup>4</sup>. Exclusive breastfeeding for at least 3 months reduces the incidence of AOM by 13% while 6 months of exclusive breastfeeding reduced the incidence of AOM to 50%<sup>35</sup>. None of the studies that explored the association of AOM in infants with duration of breastfeeding had randomized controlled designs, but when they were taken together the results showed a pattern of protection of exclusive breastfeeding<sup>9</sup>. The position of a child during breastfeeding may be better when compared to a child who is bottlefed in a supine position. The supine position and the negative pressure created in the eustachian tube during bottle-feeding may cause infants to suck excessively which may in turn lead to episodes of AOM.<sup>37</sup>

**13. Clinicians should encourage prevention of AOM by reduction of risk factors and education of parents/caregivers**

*Grade C Recommendation level 2A Evidence*

Parent's and caregivers' awareness of the disease helps prevent AOM. Knowledge and avoidance of modifiable risk factors may alleviate the burden of AOM.<sup>4</sup> In a review of studies on risk factors for recurrent AOM they found out that pacifier use, exposure to cigarette smoke, attendance at daycare facilities, craniofacial anomalies and less breastfeeding history increased the incidence of AOM recurrence.<sup>38</sup> Avoidance of exposure to tobacco smoke may also reduce the incidence of AOM in children<sup>18</sup>. Careful handwashing and use of alcoholic solutions among school-aged children were shown to reduce the incidence of AOM by 27%. On the other hand, pacifier use has been shown to increase the risk of AOM by 30%<sup>35</sup>.

**14. Probiotics are not recommended for the prevention of Acute Otitis Media in children**

*Grade C Recommendation level 2B Evidence*

A randomised, double-blind, placebo-controlled study was conducted

in order to determine whether probiotics (*Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb-12) might be effective in reducing the risk of infections in infancy. During the first year of life, nine out of thirty-two (28 %) infants who received probiotics and twenty-two out of forty (55 %) infants who received placebo encountered recurrent respiratory infections (RR 0.51 (95 % CI 0.27, 0.95); P1/4 0.022). This data suggests that probiotics may offer a safe means of reducing the risk of early acute otitis media and antibiotic use as well as reducing the risk of recurrent respiratory infections during the first year of life. However, further clinical trials are still warranted to confirm its direct effects on AOM<sup>39</sup>. Several studies have also suggested that probiotics did not prevent episodes of AOM in infants and children.<sup>40,41</sup> More studies with bigger populations and high levels of evidence are still needed in order to arrive at a definite conclusion.

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# UNILATERAL CLEFT LIP ALVEOLUS AND PALATE

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## DISCLOSURES

The members of the Philippine Academy of Facial Plastic and Reconstructive Surgery did not receive funding for the creation of these guidelines. PAFPRS has no conflicts of interest and has nothing to disclose

## INTRODUCTION

The clinical practice guidelines (CPG) on the unilateral cleft lip alveolus and palate deformity was created by the Philippine Academy of Facial Plastic and Reconstructive Surgery (PAFPRS), a study group of the Philippine Society of Otorhinolaryngology-Head and Neck Surgery, Inc. which is composed of general otolaryngologists, facial, plastic and reconstructive otorhinolaryngology surgeons from different accredited ENT training institutions as well as ENT practitioners. The views from other specialty groups such as plastic surgeons, pediatricians, dentists and families of patients were considered and included in the creation of these guidelines.

The current CPG for Cleft Lip and Palate of the University of the Philippines - Philippine General Hospital (PGH) is acknowledged as a

source and was modified for this clinical practice guideline. This report will need to be reviewed and modified periodically with new and updated knowledge.

## SCOPE OF THE PRACTICE GUIDELINE

These clinical practice guidelines are for the use of the general otorhinolaryngologists. This covers the diagnosis and management of unilateral cleft lip alveolus and palate deformities of pediatric patients (18 years and younger).

## OBJECTIVES

The objectives of the clinical practice guidelines are to (1) aid the general ENT in the diagnosis and classification (2) evaluate presurgical diagnostics (3) evaluate surgical options (4) describe the multidisciplinary cleft care team in managing patients with unilateral cleft lip alveolar and palate deformity.

## LITERATURE SEARCH

The National Library of Medicine's PubMed database was searched using keywords cleft lip, cleft palate and management. The search was limited to journals published in English for the last fifteen years, and local accredited ENT institution reports.

A total of 590 journals were initially searched and narrowed to 84 journals. Of the 84 researches used in the guideline development, thirty-three committee reports and protocols from institutions were used as guides for the formulation of the clinical practice guidelines. The articles were divided accordingly:

Meta-analysis	8
Randomized control trial	4
Non-randomized control study	11
Descriptive study	24
Committee report	33

Four unpublished researches were included due to their relevance as they provided local data for the recommendations. All materials were assessed for relevance and classified according to levels of evidence and grades of recommendations based on guidelines from the Oxford Centre for Evidence-Based Medicine.<sup>1</sup>

The guideline development group was divided into three subgroups to formulate key recommendations on diagnosis and pre-surgery concerns, surgical and multidisciplinary management. A series of meetings over one year were performed for writing, discussion and appraisal of recommendations prior to external review and publication.

## DEFINITIONS

Cleft lip and palate is a congenital anomaly with a wide range of presenting variety of forms and combinations. It is the failure of fusion of embryonal facial clefts. Cleft lip ranges from notching of the lip to a complete cleft, involving the floor of the nose. It may be associated with a cleft of the primary palate (alveolus/pre-maxilla) and with clefts of the

secondary palate (hard and soft palate). Cleft lip can further be described as unilateral or bilateral, complete or incomplete.<sup>2</sup>

Primary surgical procedures are the initial interventions designed to correct the deformities associated with the cleft lip and palate. These include: cheiloplasty, alveoloplasty, rhinoplasty, and palatoplasty.

Primary rhinoplasty is the initial procedure that is usually done during the primary cheiloplasty. This involves the release and repositioning of the deformed alar cartilage and/or columella. The aims of primary rhinoplasty are to achieve normalization of the nose, i.e., symmetry, by lengthening the cleft side columella, elevating the lower lateral cartilage, and shortening or lifting the cleft side heminose.<sup>2</sup>

Secondary surgical procedures are the follow-up interventions designed to correct the residual deformities associated with the cleft lip and palate. These include alveolar bone grafting, palate rerepair or velopharyngoplasty, definitive rhinoplasty, lip revision and orthognathic surgery.<sup>2,3</sup>

Definitive rhinoplasty is a nasal procedure to correct residual nasal deformity done once approximate facial maturity is achieved.<sup>2,3</sup>

#### PREVALENCE

Cleft lip and palate represents the second most frequently occurring congenital deformity. The incidence of cleft lip and palate varies considerably according to race. The incidence among Caucasians is 1:1000 live births, while American Indians is 3.6:1000 live births. The incidence for Asians is slightly higher, Japanese 2.1:1000 live births and Chinese, 1.7: 1000 live births.<sup>4</sup>

Based on an 8-year study done by the Corazon Locsin Montelibano Memorial Regional Hospital in 1997, the prevalence of cleft lip with or without cleft palate is 2 per 1000 live births. Based on the Philippine Oral Cleft registry in 2008, the incidence is 0.46 per 1000 live birth.

According to a census by the Philippine Birth Defects Registry Project from 1999-2001, cleft lip and palate is the third most common birth defect in the Philippines (first is multiple congenital anomalies, second is ankyloglossia). A total of 110 cases of cleft lip and palate were tallied, 5.6:10,000 live births.<sup>5</sup>

In a census done in Philippine General Hospital from 1996-2000, there were 378 cases of bilateral cleft lip (associated cleft palate not specified), 208 cases of cleft lip with palate and 188 cases of cleft lip alone. In 2002, an average of 21 CLAP patients per month was seen at the ORL outpatient clinic of the Philippine General Hospital. Four to eight cleft operations per month were performed.<sup>6</sup>

Based on a study done by the Manila Doctors Hospital Department of Otorhinolaryngology on their patients with cleft lip and palate from 2004 to 2014, a demographic profile was developed. A total of 178 patients were seen, with an overall sex ratio of 1.17 male: 1 female. Eighty percent of the cases were unilateral, while 20% were bilateral. Of the patients with bilateral clefts, 78% had a combined cleft plate and lip deformity. Of

the patients with unilateral clefts, majority were cleft palate deformities (37%) and cleft lip deformities (21%). Of the patients with isolated unilateral cleft lip deformity, 75% were left-sided.<sup>7</sup>

#### RECOMMENDATIONS ON THE DIAGNOSIS OF CLEFT LIP AND PALATE

##### 1. History-taking is essential in the evaluation of patient with cleft lip and palate deformity.

*Grade D Recommendation Level 5 Evidence*

Risk factors for cleft lip and palate include maternal alcohol consumption, reduced folic acid concentrations, and genetic linkage. Based on a study by Bezerra et al., maternal alcohol consumption and reduced folic acid concentrations increases the risk for non-syndromic cleft lip and palate.<sup>8</sup>

##### 2. An initial Head and Neck examination is essential in the evaluation of patient with cleft lip and palate deformity.

*Grade D Recommendation Level 5 Evidence*

The head is inspected for symmetry. The auricle and the external ear canal are checked for development and location. A facial analysis is helpful to identify abnormalities of facial symmetry and harmony. Otologic examination includes pneumatic otoscopy and tuning fork tests. Cleft palate is commonly associated with Eustachian tube dysfunction due to an abnormal insertion of the levator and tensor veli palatini muscles in the posterior margin of the hard palate. Anterior and posterior rhinoscopy will identify clefting, septal abnormalities, intranasal masses and choanal atresia. Oral cavity examination will reveal any cleft, dental arch abnormalities and tongue anomalies such as bifid tongue, macroglossia, glossoptosis, or lingual thyroid. In addition, malocclusion, hemifacial hypertrophy or atrophy, and facial clefting are documented. The upper airway tract is evaluated by assessing the adequacy of phonation, cough, and deglutition, and by auscultating and palpating the neck.<sup>9</sup>

##### 3. The Thallwitz Classification in the diagnosis of CLAP deformities is recommended.<sup>10</sup> For ICD-10 and PHIC use, the Veau classification is recommended.

*Grade D Recommendation Level 5 Evidence*

Cleft lip and palate patients will be classified according to the Thallwitz nomenclature and ICD-10 system. The institutions using the Thallwitz are the following: Philippine General Hospital, Manila Doctors Hospital, Far Eastern University Medical Center, Quezon City General Hospital, Veteran's Memorial Hospital, St. Luke's Medical Center, University of the East Ramon Magsaysay Memorial Medical Center, Quirino Hospital, and East Avenue Medical Center.

The Veau system classifies cleft lip and palate deformities into four classes, depending on whether the primary and/or secondary palates are affected and by laterality.<sup>11</sup> This classification system is used by the ICD and PHIC. (Table 1)

**Table 1.** Veau system of classification

Veau Class I	Incomplete cleft, soft palate only (no unilateral/bilateral designation)
Veau Class II	Hard and soft palate, secondary palate only (no unilateral/bilateral designation)
Veau Class III	Complete unilateral cleft including lip (primary and secondary palates)
Veau Class IV	Complete bilateral cleft

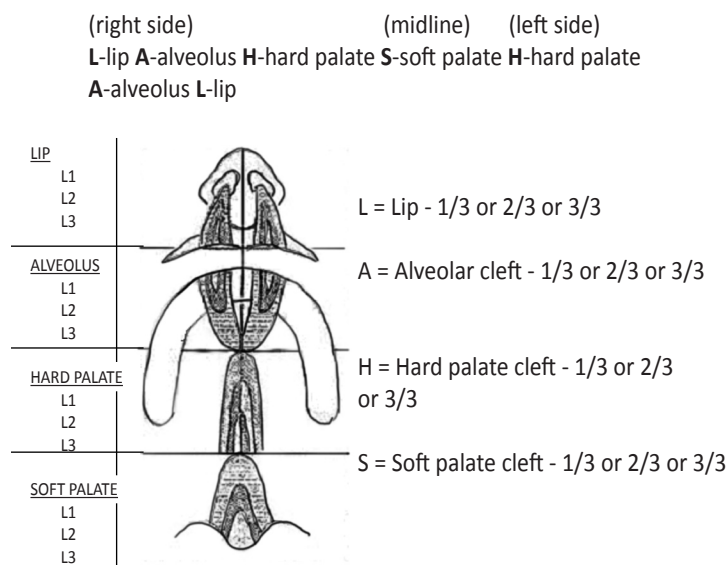
The **ICD-10 system** is an international standard of coding. Various descriptions of cleft deformities and their codes are seen in Table 2.

**Table 2.** ICD-10 system

Cleft hard and soft palate with cleft lip, bilateral	Q374
Cleft hard and soft palate with cleft lip, unilateral	Q375
Cleft hard palate with cleft lip, bilateral	Q370
Cleft hard palate with cleft lip, unilateral	Q371
Cleft hard palate with cleft soft palate, bilateral	Q354
Cleft hard palate with cleft soft palate, unilateral	Q355
Cleft hard palate, bilateral	Q350
Cleft hard palate, unilateral	Q351
Cleft lip	Q36
Cleft lip, bilateral	Q360
Cleft lip, medial	Q361
Cleft lip, unilateral	Q369
Cleft palate	Q35
Cleft palate with cleft lip	Q37
Cleft palate, medial	Q356
Cleft palate, unspecified, bilateral	Q358
Cleft palate, unspecified, unilateral	Q359
Cleft soft palate with cleft lip, bilateral	Q372
Cleft soft palate with cleft lip, unilateral	Q373
Cleft soft palate, bilateral	Q352
Cleft soft palate, unilateral	Q353
Cleft uvula	Q357

The Thallwitz nomenclature (commonly known as the LAHSHAL) is a descriptive classification since site, size, extent and type of cleft are considered. Severity of the deformity is objectively documented and the recorded findings can easily be stored into a computer for data analysis. Each area is divided into thirds, and cleft defects are graded as to extent of affected areas. Grading is done for both sides as shown in Figure 1.

**Figure 1.** Thallwitz nomenclature



**RECOMMENDATIONS ON DIAGNOSTICS AND PRE-SURGERY**

**1. Early second trimester detection of CLAP deformity through ultrasonography is recommended.**

*Grade C Recommendation Level 4 Evidence*

The second trimester ultrasound recommended can be done in conjunction with the ultrasound commonly recommended by obstetricians to screen for congenital anomalies. Early detection of a cleft deformity can prepare the family for future interventions, be it medical, surgical, psychological, or economic.<sup>12</sup>

**2. Folic acid supplementation is recommended prior to conception.**

*Grade A Recommendation, Level 1A Evidence*

Based on the 2010 Cochrane review for periconceptional folic acid supplementation for the prevention of cleft deformities, folic acid supplementation is favorable.<sup>13,14</sup>

**3. While Otoacoustic Emission (OAE) with or without Auditory Brainstem Response (ABR) is already done for newborn hearing screening, Tympanometry is recommended to be added for patients with cleft palate.**

*Grade B Recommendation, Level 2B Evidence*

Paradise, et al. developed the term “universality of otitis media in cleft palate children” after demonstrating that 96% of cleft patients had middle ear effusion hence evaluation of hearing status including newborn hearing screening is necessary.<sup>15,17</sup>

- 3.1 According to a study done by Dhillon in 1988 and Robinson in 1992, 92% - 97% of patients with cleft palate develop otitis media with effusion.<sup>16,17</sup> In a study done at Manila Doctors Hospital, 100% of patients with cleft palate have otitis media with effusion on both ears.<sup>18</sup>
- 3.2 Based on a study by Handzik-Cuk et al., type B tympanograms are associated with 21-40-dB hearing loss in patients with cleft lip and palate.<sup>19</sup> Otitis media with effusion is associated with patients with cleft palate due to velopharyngeal insufficiency.<sup>19</sup>
- 3.3 It is established that pediatric patients with effusion develop significant hearing loss that could affect speech and language. These children are set to a mild to moderate hearing loss that averages about 25 dbHL as a result of the fluid in the middle ear space. Such occurrence will impair the ability to hear speech, and thereby encode information ineffectively and inaccurately, from which language develops. Speech at a conversational level will be difficult for these patients that will lead to poor interaction, then subsequent decreased opportunities to learn language.<sup>20</sup>
- 3.4 An otoacoustic emission test (OAE) or an auditory brainstem response (ABR) test is used as hearing screening in newborn with cleft lip and palate.<sup>21</sup>
- 3.5 A retrospective study of middle ear effusion and treatment outcomes with cleft palate patients at the Connecticut Children's Medical Center from 2005 to 2009 by Szabo, et al. revealed that 82% of cleft palate passed the newborn hearing screening. 98% developed middle ear fluid requiring at least one set of tubes; while 75% only required 1-2 sets of tubes before resolving the eustachian tube dysfunction sufficiently that OME did not reaccumulate.<sup>22,23</sup>

**4. Pre- and post-operative photodocumentation of patients with cleft lip and palate deformity may aid the clinician in surgical planning and assessing surgical outcomes.**

*Grade C Recommendation, Level 4 Evidence*

Based on literature, there are no standardized views for pre and post-operative photodocumentation of cleft lip and palate patients. However, there are some studies who have used frontal and submental photographic views for post-operative assessment of patients.<sup>24, 25, 26</sup>

**5. Cephalometric radiographs for patients ages 6 and above (start of mixed dentition) and candidates for alveolar bone grafting is recommended.**

*Grade C Recommendation, Level 4 Evidence*

Cephalometric radiographs aid in surgical planning for alveolar bone grafting especially for patients ages 6 and above who already start to have mixed dentition.<sup>27</sup>

**6. Pediatric evaluation and clearance prior to surgical intervention to assess for other co-morbid conditions is recommended.**

*Grade B Recommendation, Level 2 Evidence*

For any surgical procedure, pre-operative evaluation and clearance is recommended.<sup>28</sup>

**7. Presurgical application of Nasoalveolar Molding (NAM) for cleft palate is recommended**

*Grade B Recommendation, Level 2B Evidence*

The use of nasoalveolar molding has proven to be an efficient method for reducing cleft width and improving nasal shape and symmetry in unilateral clefts. The immediate success of the therapy facilitates cleft surgery immensely. Regardless of the cleft width, preoperative narrowing of the lip and alveolar segments, nasal shaping and columella lengthening help to reduce tissue tension and therefore improve surgical outcome by minimizing wound healing disturbances and scarring.<sup>29</sup>

**SURGICAL MANAGEMENT OF THE UNILATERAL CLEFT LIP-ALVEOLUS-PALATE DEFORMITY**

The aim of cleft surgery is to restore the entire cleft defect to as near a normal anatomy as possible. It is divided into primary and secondary surgical procedures.

**RECOMMENDATIONS FOR PRIMARY SUGICAL PROCEDURES**

**1. Cheiloplasty is done as early as three months**

*Grade D Recommendation, Level 5 Evidence*

Early cheiloplasty is not done as it has been proven to cause maxillary retrusion and reduced maxillary length.<sup>30</sup> Performing the procedure at three months or later allows the child to achieve significant maxillary growth, to allow for more tissue availability for the repair, more time for parent-child bonding, and more time for the parents to gain a better understanding and acceptance of the child's congenital deformity. Rotation advancement for both complete and incomplete unilateral cleft lip repair is the most common technique among training institutions previously cited.

**2. Alveoloplasty (soft tissue only) can be done with primary cheiloplasty or until the ideal age for bone grafting is reached**

*Grade C recommendation, Level 4 Evidence*

Early alveoloplasty is not done as it has been found to result in reduced maxillary height.<sup>31</sup> The procedure is delayed to allow significant maxillary growth and to allow for more tissue availability for the repair. The alveolar bone grafting procedure is postponed until 7 to 9 years old because it is at this time where the root of the permanent canine has formed 1/3 to 2/3, and the crown is still partially covered by bone.<sup>32,32,34</sup> At this age, there is minimal retrusion noted as opposed to it being done earlier.

**3. Primary rhinoplasty can be done with primary cheiloplasty or until as early as 14 years old for females and 16 years old for males which is the ideal age for definitive rhinoplasty.**

*Grade B Recommendation, Level 2B Evidence*

Primary rhinoplasty occurs with the initial lip repair as previous beliefs on early nasal surgery interfering with nasal and midface growth have been overturned.<sup>35,36</sup> The benefit of early intervention allows for an earlier restoration of nasal shape with the potential for more symmetric nasal growth as well as to spare the child the psychosocial impact of

ridicule and bullying.<sup>37,38</sup> Definitive rhinoplasty is done after facial growth is completed, which is around 14 years old in females and 16 years old in males.<sup>39,40</sup>

**4. Palatoplasty can be done at 12 to 18 months.**

*Grade C Recommendation Level 4 Evidence*

Surgery is ideally based on stage of phonemic development or articulation age, and not chronologic age.<sup>41</sup> Surgery is delayed to a time after 12 months so that the repair required to establish a competent velopharyngeal sphincter is minimized. Surgery should be performed by 18 months to minimize development of irreversible pathologic compensatory speech patterns.<sup>41,42</sup> Although some studies have advocated early surgical intervention, there is insufficient evidence that early palatal closure is superior to surgery performed later. In fact, early palatoplasty produces maximal growth inhibition in all dimensions, and the surgical region has been shown to grow more slowly than the surrounding tissue, possibly due to the extent of scar contracture.<sup>43,44</sup>

**5. Ventilation tube insertion can be done as indicated.**

*Grade B Recommendation, Level 2B Evidence*

Otitis media with effusion was found in 92-100% of patients with cleft palate to have otitis media with effusion.<sup>45</sup>

Patients with type B tympanogram (less than 0.35 compliance) are recommended to undergo myringotomy with ventilation tube insertion. Randomized trials show a mean 62% relative decrease in effusion prevalence after insertion of ventilation tubes.<sup>46</sup> Palatoplasty and ventilation tube insertion solved 48.7% of ears with otitis media with effusion.<sup>47</sup> Palatoplasty and ventilation tube insertion changed the pressure conditions in the middle ear cavity raising the hearing level to about 17 decibels in the middle-ear-diseased cleft palate patients. Patients who underwent palatoplasty alone did not show changes in middle ear function.<sup>48</sup>

A study done at Manila Doctors Hospital comparing otitis media with effusion using tympanometry among patients with cleft palate who underwent either palatoplasty with ventilation tube placement versus ventilation tube placement alone revealed statistically significant improvement in the outcome on repeat tympanometry in terms of middle ear condition with palatoplasty and ventilation tube placement (combined procedure), and likewise with ventilation tube placement alone. However, it noted better results are obtained in favor of doing the combined procedure with a statistically significant difference between the pre- and post-surgery compliance in tympanometry.<sup>49</sup>

Ventilation tubes are known to ventilate the middle ear for an average of 6 to 14 months which would improve hearing loss to a mean of 6 to 17 dB.<sup>50</sup>

Recommended follow-up intervals for the evaluation of otitis media with effusion among patients with cleft palate deformities who underwent palatoplasty and ventilation tube insertion are varied. The American Academy of Pediatrics Section on Otolaryngology has published guidelines for follow-up at intervals of no longer than 6 months<sup>51</sup> (Table 3). A

follow-up tympanometry was done after 12 months in studies previously cited and showed considerable changes in compliance for both groups even after extrusion.<sup>52,53</sup>

**Table 3.** Timing of Primary Surgical Procedures

Procedures	Timing
Cheiloplasty	As early as 3 months
Alveoloplasty (soft tissue only)	Can be done with primary cheiloplasty or until the ideal age for bone grafting is reached
Primary rhinoplasty	Can be done with primary cheiloplasty or until the ideal age for definitive rhinoplasty is reached
Palatoplasty	12 to 18 months
Ventilation tube insertion	As indicated

**RECOMMENDATIONS FOR SECONDARY SURGICAL PROCEDURES**

The secondary surgical procedures aim to improve on the aesthetic and other functional problems.

**1. Alveolar bone grafting can be done as indicated at 7 to 9 years old in consultation with the Orthodontist.**

*Grade B recommendation, Level 2B evidence*

The advantages of alveolar bone graft in an alveolar cleft have been noted to be the following: (1) assists in the closure of the buccoalveolar oronasal fistula, (2) provides bony support for unerupted teeth and teeth adjacent to the cleft, (3) forms a continuous alveolar ridge to facilitate orthodontic correction of malocclusion, (4) supports the nasal floor and the base of the alae to improve nasal aesthetics.<sup>54</sup>

Mixed dentition bone grafting does not affect subsequent vertical and antero-posterior development of the maxilla in complete unilateral cleft lip and palate patients during the first postoperative years in several retrospective cephalometric studies.<sup>55</sup>

**2. Palate re-repair/velopharyngoplasty can be done as indicated or whenever recommended by a speech therapist.**

*Grade B recommendation Level 2B evidence*

Velopharyngoplasty is an important method for repair of velopharyngeal insufficiency in patients with cleft palate. Speech quality is improved but an intensive interdisciplinary cooperation of all specialists involved is necessary.<sup>56</sup>



A systematic review indicated an increased incidence of velopharyngeal insufficiency as revealed by higher odds of secondary operations in the straight-line intravelar veloplasty repair of unilateral cleft lip-cleft palate when compared to the Furlow z-plasty.<sup>57</sup>

**3. Definitive rhinoplasty can be done as indicated, as early as 14 years old for females and 16 years old for males.**

*Grade C Recommendation Level 4 Evidence*

Definitive rhinoplasty if indicated is performed after the completion of maxillary and nasal growth, which usually occurs at 14-16 years of age in women and 16-18 years of age in men. The goals of this surgery are final creation of lasting symmetry, achieving definition of the nasal base and tip, relief of nasal obstruction, and management of nasal scarring and webbing.<sup>58</sup>

**4. Lip revision can be done as indicated but not earlier than 3 months from previous lip surgery.**

*Grade C Recommendation, Level 4 Evidence*

Traditionally scar revision is performed 6-12 months after repair. However, a repair that is uneven, or is obviously poorly positioned may be revised as early as 3 months after the previous lip surgery. If it is possible to tell early that the scar will not improve with maturation, early revision with realignment may allow it to mature more rapidly.<sup>59</sup>

In a review of 750 patients with unilateral cleft lip, secondary reconstruction was performed in 35% of patients.<sup>60</sup>

**5. Orthognathic surgery can be done as indicated as early as 14-16 years old for females and 16-18 years old for males**

*Grade B Recommendation Level 2B Evidence*

Orthognathic surgical correction is planned at skeletal maturity usually at 14-16 years of age in women and 16-18 years of age in men, following orthodontic preparation.<sup>61</sup> (Table 4)

**Table 4. Timing of Secondary Surgical Procedures**

Procedure	Timing
Alveolar bone grafting	7 to 9 years in consultation with the Orthodontist
Palate re-repair / velopharyngoplasty	As indicated or whenever recommended by a speech therapist
Definitive rhinoplasty	As early as 14 years old for females and 16 years old for males
Lip revision	As indicated but not earlier than 6 months from previous lip surgery
Orthognathic surgery	As early as 16 years old for females and 18 years old for males

**RECOMMENDATIONS ON A MULTIDISCIPLINARY CLEFT CARE TEAM**

Cleft patients are best managed in an environment of a multidisciplinary cleft care team which includes pediatricians, cleft surgeons, otorhinolaryngologists, orthodontics, prosthodontics, nutritionists, clinical otologists and audiologists, speech pathologists, clinical psychologists, and genetic counselors.<sup>62</sup> The team should include the family of patients with cleft deformities as well. Institutions with programs for patients with cleft deformities and their families should strive to complete their multidisciplinary teams to ensure the comprehensive and holistic care of these patients.

**1. Pediatricians should be a part of the multidisciplinary CLAP team from birth to adolescence to oversee their general well-being and proper growth and development.**

*Grade D Recommendation, Level 5 Evidence*

- 1.1 Pediatric management begins in the hospital nursery by ruling out possible associated anomalies.<sup>63</sup>
- 1.2 Pediatricians are in a unique position to help prepare children and their families for surgery and help the perioperative team optimize care. Communication about conditions related to increased risk in the OR and aiding the family to advocate for their child in a stressful situation are valuable contributions to the preoperative preparation of the pediatric patient.<sup>64</sup>
- 1.3 Since pediatricians oversee the well-being of the child including the normal growth and development after surgery, frequent monitoring is required for children who may be at risk for growth failure, delayed development, or any other significant problems.<sup>64</sup>

**2. Cleft surgeons (Otolaryngologist, Plastic Surgeons, Oral and maxillofacial surgeons) with explicit documentation of training in cleft care should perform cleft lip and palate surgery, scar revisions, and rhinoplasty.**

*Grade D Recommendation, Level 5 Evidence*

- 2.1 Explicit documentation here entails “documented evidence of residency training (as an operating surgeon, not as an assistant) in lip, palate and nasal procedures”<sup>62</sup>

**3. Orthodontics (dentofacial orthopedics) and dental care should be an integral part in the rehabilitation of the child with cleft lip and palate and can be initiated at any age from birth to adolescence<sup>65,66</sup>**

*Grade B Recommendation, Level 3 Evidence*

- 3.1 In dental rehabilitation, the dentist provides oral health information and should be able to follow the child with cleft lip and palate since the first months of life until establishment of mixed dentition, craniofacial growth and dentition development.<sup>65</sup>
- 3.2 The orthodontist monitors the craniofacial growth and development and corrects malocclusions, which are more complex compared to patients without clefts<sup>66</sup>

**4. Prosthodontist should be an essential part in care of the child with alveolar and palate deformity in creating nasoalveolar molding devices (NAM). NAMS should be done in infancy to narrow and prevent further widening of the cleft palate.**

*Grade B Recommendation, Level 3 Evidence*

- 4.1 Feeding instructions, molding appliance fitting and feeding plate modification are done in infancy. A study by Konst showed that children treated with intra-oral prosthesis during their first year of life followed a more normal path of phonological development between 2 and 3 years of age.<sup>67</sup>
- 4.2 The combined use of palatal obturator and lactation education reduced feeding time, increased volume intake and was associated with good growth.<sup>68</sup>

**5. Breastfeeding is encouraged for patients with cleft lip and palate**

*Grade A Recommendation, Level 1A Evidence*

- 5.1 Mothers should be counseled about likely breastfeeding success. Where direct breastfeeding is unlikely to be the sole feeding method, the need for breastmilk feeding should be encouraged, and when appropriate, possible delayed transitioning to breastfeeding should be entertained.<sup>69</sup>

**6. A nutritionist is recommended to be part of the team for feeding instructions and support for new parents of babies with cleft lip and palate deformity.**

*Grade D Recommendation, Level 5 Evidence*

- 6.1 The patient with cleft lip and/or palate deformity is faced with nutritional problems beginning at birth because of the difficulty in feeding resulting from the altered anatomical structures. Nutritional deficiencies lead to inadequate nourishment and poor weight gain in the young patient that can cause delays in any contemplated surgery for the repair of cleft deformities.<sup>70</sup>
- 6.2 Nutritionists provide feeding guidance beginning in the neonatal period by giving information concerning the feeding resources available for children with clefts, including breastmilk whenever necessary by use of feeding bottle, cup, spoon or feeder; including the appropriate posture during feeding, and pre- and post-feeding oral hygiene.<sup>71</sup>
- 6.2 Growth parameters are monitored closely during the first week of life and over the long term.<sup>72</sup>
- 6.3 In a study done at Manila Doctors Hospital to determine the effectiveness of integrating clinical nutrition management with individualized nutrition counseling in the CLAP surgical mission, the following were the findings: all patients had less than normal BMI pre-operatively and statistically significant weight gain was seen in patients with individualized nutrition counseling.<sup>73</sup>

**7. A speech pathologist is recommended for the management of**

**velopharyngeal insufficiency after cleft palate surgery to obtain normal articulation.**

*Grade B Recommendation, Level 3B Evidence*

- 7.1 Speech therapy can begin as early as 2 weeks following surgery, if the patient feels well and the surgeon agrees.<sup>74</sup>
- 7.2 Following cleft palate closure, speech is usually evaluated at regular 4-6 month intervals, or as needed, in order to ensure the continued development of articulation skills and the use of adequate velopharyngeal function. In general, speech therapy is usually initiated anywhere from 20 months to 2 years of age.<sup>74</sup>
- 7.3 Children ages 3 through 5 are more receptive to acquiring new speech patterns and correcting abnormal speech patterns than older children. They are in a critical period of brain development, making the brain more receptive to learning these skills.<sup>74</sup>
- 7.4 When oral-nasal resonance balance and articulation were combined in each child, those children who achieved *both* normal oral-nasal resonance balance and normal articulation (per age expectancy) amounted to 88%.<sup>75</sup>

**8. Clinical audiologists and otologists are recommended to be part of the team to determine the hearing status and evaluate of the presence of middle ear diseases among cleft palate patients.**

*Grade A Recommendation, Level 1B Evidence*

- 8.1 Otoacoustic Emission (OAE) with or without Auditory Brainstem Response (ABR) and Tympanometry can be done for newborns with cleft palate as previously recommended.<sup>76</sup>
- 8.2 Paradise, et al developed the term “universality of otitis media in cleft palate children” after demonstrating that 96% of cleft patients had middle ear effusion hence evaluation of hearing status including newborn hearing screening is necessary.<sup>15,77</sup>
- 8.3 An otoacoustic emission test (OAE) or an auditory brainstem response (ABR) test is used as hearing screening in newborn with cleft lip and palate according to Tropper, et al.<sup>21,77</sup>

**9. A clinical psychologist is recommended to be part of the team to work with the child, parents and the family to ensure normal functioning by providing intervention on issues such as parental adjustment and cleft child self-esteem.**

*Grade C Recommendation, Level 4 Evidence*

- 9.1 The earliest intervention may help to improve social competence and reduce stress beginning in the antenatal or perinatal stages of care when working with parents and significant family members.<sup>78</sup>
- 9.2 Emotional effects and psychological aspects of cleft lip and palate deformities and their treatment must be considered. Understanding of the causes of cleft deformities is clouded by myths in the community. This causes increased anxiety among the child, parents and the rest of the family.<sup>78</sup>

**10.A genetic counselor is recommended to be part of the team to help the family gain understanding of the predisposing factors and determine risk of recurrence.**

*Grade D Recommendation, Level 5 Evidence*

A comprehensive clinical genetic evaluation is a key component in the management of cleft lip and palate and should include diagnosis, recurrence risk counseling and counseling regarding prognosis.<sup>62, 64, 78</sup>

**11.The family of patients with cleft deformities which may include parents, guardians and older siblings are recommended to be part of the multidisciplinary team.**

*Grade D Recommendation, Level 5 Evidence*

The family of patients with cleft deformities as part of the multidisciplinary team should be properly oriented in order to empower them in decision-making and the day-to-day care and long-term interventions needed by the patients.<sup>79</sup>

**RECOMMENDATIONS ON OUTCOMES MONITORING**

Better recommendations can be developed with better evidence of reported outcomes of care. The following are recommendations on outcomes monitoring for Unilateral Cleft Lip Alveolus and Palate care.

**1. Assessment parameters should be standardized for the different stages of unilateral cleft lip alveolus and palate care.**

*Grade D Recommendation, Level 5 Evidence*

Various instruments are available in literature, however, there is no single instrument available that comprehensively assess perceptions of children with cleft deformities. Suggested parameters like aesthetics and associated conceptual and perceptual consequences, functional deficits in chewing, breathing, and vocal resonance, and treatment benefits is recommended to be included in a quality of life instrument.<sup>80</sup>

Evaluating satisfaction must be the fundamental goal in any team with genuine concern for the well-being of people in their care. The challenge is to improve these efforts through the development of more robust and revealing instruments that can be meaningfully used in the future international comparison.<sup>81</sup> A study from Manila Doctors Hospital evaluated the treatment and delivery of services to indigent patients with cleft lip and palate deformities. It included a questionnaire to determine patient and family satisfaction, questionnaire for participant physicians, and review of outcomes (e.g. complications symmetry, revisions).<sup>82</sup>

For purposes of documentation and outcome analysis, a standardized video recording to assess cleft surgery outcomes has been suggested.<sup>83</sup>

Several inter-center studies have cited and used nasolabial aesthetic outcome evaluation and have been shown to provide a reasonably reliable and reproducible rating system. The system allows sensitive rating of the individual feature of the nasolabial complex and appears workable in practice.<sup>84</sup>

**2. A panel of assessors is the best method to adopt in the evaluation of outcomes.**

*Grade D Recommendation, Level 5 Evidence*

Bardach et al. evaluated the treatment outcome in bilateral cleft lip and palate with a multidisciplinary approach. The evaluation was comprised of a plastic surgeon, an orthodontist, an otolaryngologist, and a speech pathologist. This is the first reported attempt at a multidisciplinary evaluation of a center’s treatment management of complete bilateral cleft lip and palate with no associated malformations.<sup>85</sup>

Professionals and lay people rated nasolabial appearance differently. Their ratings did not correlate with the results from a self-assessment questionnaire of patients with UCLP and controls. The current results suggest that judgement of nasolabial appearance in adults treated for UCLP differs among professionals, laymen, and patients. This should be considered in the decision-making process for secondary surgical treatment of signs of clefts.<sup>86</sup>

**3. Institutional outcomes should be reported as outcomes researches for the medical community to contribute in improving the comprehensive multidisciplinary care for patients and families with unilateral cleft lip alveolus and palate care.**

*Grade D Recommendation, Level 5 Evidence*

A reliable measure of the facial appearance of patients with cleft lip and palate is essential if meaningful research into surgical outcome is to progress. Assessment of facial appearance should be used in conjunction with assessment of speech, psychosocial adjustment, dental arch relationships, and conventional cephalometric analysis.<sup>84, 87</sup>

Intercenter and multicenter studies are useful methods for evaluation treatment outcomes. The inclusion criteria should be uniform and the assessment should be approached from multiple perspectives including facial appearance, speech, craniofacial morphology and occlusion.<sup>88</sup>

**RECOMMENDATIONS ON POST-OPERATIVE CARE**

The goal of any postoperative plan should be to minimize complications and return the child to normal life as quickly as possible.

**1. Minimal hospital stay and early discharge after surgery is recommended.**

*Grade D Recommendation, Level 5 Evidence*

Katzel et al. evaluated practices of American Cleft Palate-Craniofacial Association surgeons and cleft teams in relation to length of hospital stay following cleft repair and postoperative complications. The findings in this study suggest cleft patients are discharged early, within 1 or 2 days postoperatively. Several studies support the safety of this type of early discharge specifically in non-syndromic patients.<sup>89</sup>

The financial benefits to patients and the health care system because of early discharge following cleft palate repair have also been documented in the literature.<sup>89</sup>

**2. Immediate return to breastfeeding after surgery is recommended.**

*Grade D Recommendation, Level 5 Evidence*

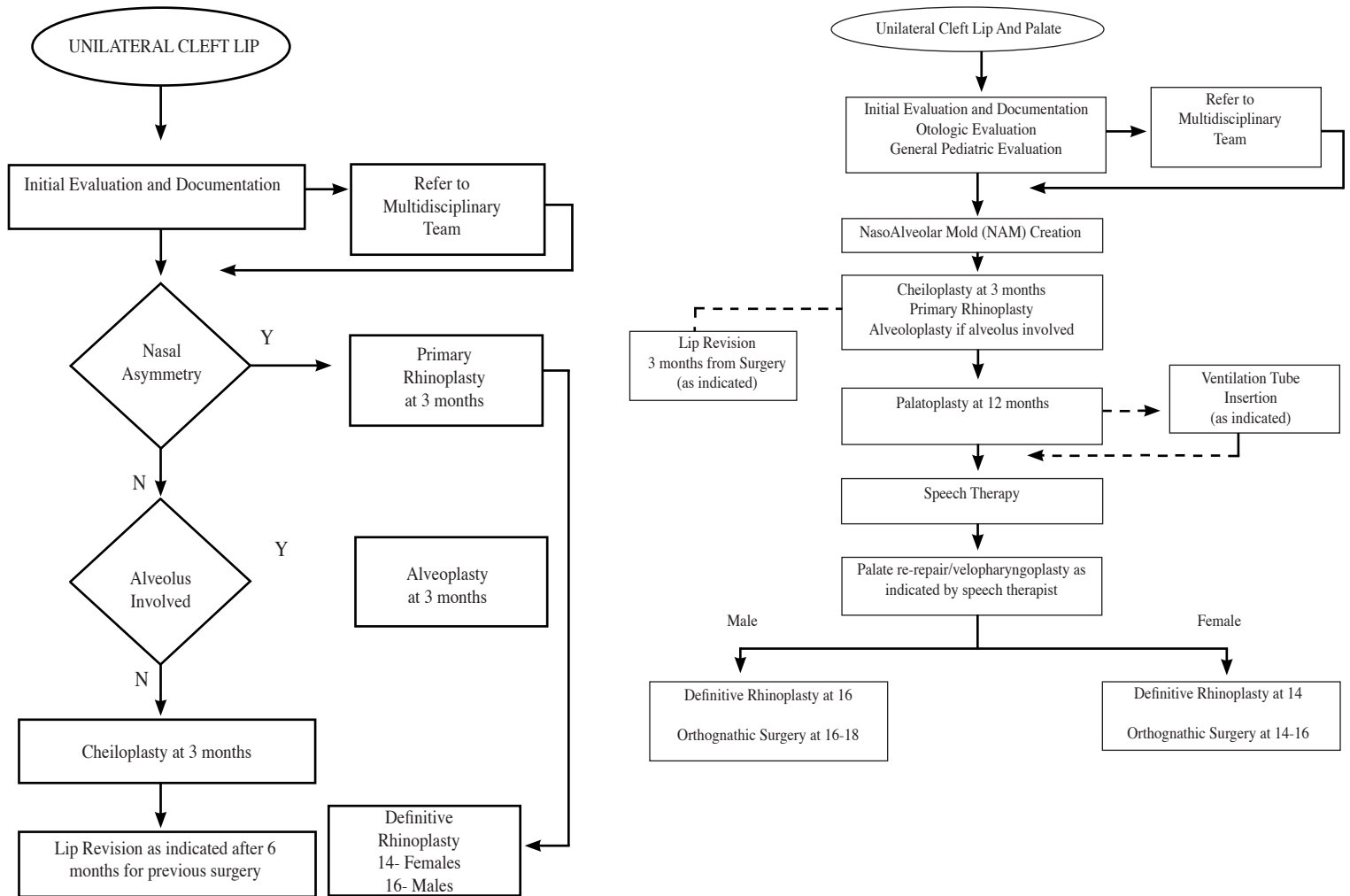
Postoperative feeding remains somewhat more controversial as to the length of time until return to normal diet and type of bottle recommended or use of spoon or syringe feeding. American Cleft Palate-Craniofacial Association surgeons and cleft teams were more in agreement regarding the immediate return to breast-feeding after surgery.<sup>90</sup>

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APPROACH TO UNILATERAL CLEFT LIP AND PALATE



# ALLERGIC RHINITIS IN ADULTS

Philippine Academy of Rhinology

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## PURPOSE

This clinical practice guideline (CPG) is intended to describe appropriate care based on the best available scientific evidence and broad consensus for allergic rhinitis in adults. It aims to reduce inappropriate variations in clinical practice and to highlight management principles unique to the specialty of Otorhinolaryngology in the Philippines.

## TARGET POPULATION, SETTING AND PROVIDERS OF CARE

This CPG is for use by the Philippine Society of Otolaryngology-Head and Neck Surgery. It covers the diagnosis and management of Allergic Rhinitis (AR) in adults.

## OBJECTIVES

The objectives of this guideline are (1) to provide the requisite criteria for the diagnosis of allergic rhinitis; (2) to describe the current diagnostic techniques; and (3) to recommend management options relevant to the local setting.

## METHODOLOGY

The panel was asked to review the previously published guideline for allergic rhinitis. Data from scientific studies were presented in an analytical framework in the initial panel meeting, and revisions and recommendations were formulated. In the present document, an extensive search of MEDLINE, National Library of Medicine's PubMed database, and Agency for Healthcare Research and Quality (AHRQ) Evidence Report and Technology Assessment was done using the keyword "Allergic rhinitis", exploded to include *definition/classification, prevalence/epidemiology, diagnosis, and therapy*. The search was limited to articles involving adult (19 years old and above) humans, and those published in English from 2010 to 2015. The search yielded 885 articles which included the following:

Meta-analysis/Systematic Reviews:	66
Randomized controlled trial:	295
Consensus report/ CPG:	4

Additionally, older journal articles, unpublished literature and oral communications were included. A draft of the evidence-based recommendations (EBR) was collated and presented by the panel to the general assembly of ORL-HNS specialists.

This guideline will undergo review and updating five (5) years after publication, or earlier, depending on the emergence of new information.

## FUNDING AND DISCLAIMER

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## COMPETING INTERESTS

All authors have stated that they have no competing interests.

## DEFINITION AND PREVALENCE OF ALLERGIC RHINITIS

**Allergic rhinitis (AR)** is defined as chronic or recurrent IgE-mediated inflammation of the nasal mucosa. Primary symptoms include rhinorrhea, sneezing, nasal itching, nasal congestion and postnasal drainage. It may be associated with other symptoms such as frequent throat clearing, eye itching, tearing, eye redness, palatal itching, impaired sense of smell (and taste), fatigue, impaired concentration and reduced productivity.<sup>(1-3)</sup> It can be classified as intermittent or persistent, and as mild or moderate-severe.<sup>(3)</sup> **Intermittent AR** is characterized by symptoms of less than four (4) days a week OR less than four (4) consecutive weeks. **Persistent AR** has symptoms occurring for more than four (4) days a week AND for more than four (4) weeks.<sup>(3)</sup> Using a conservative estimate, AR occurs in over 500 million people around the world. Its prevalence is increasing in most countries. In the Philippines, prevalence ranges from 18% in urban areas to 22.1% in rural areas and from 26% in young children to 32% in adolescents.<sup>(4)</sup>

## RECOMMENDATIONS ON THE DIAGNOSIS OF ALLERGIC RHINITIS IN ADULTS

**1. The diagnosis of AR is strongly considered in the presence of the following symptoms: nasal itching, sneezing, rhinorrhea, and/or nasal congestion or obstruction, triggered by allergen exposure. Symptoms may be associated with conjunctival redness, itchy and/or teary eyes.**

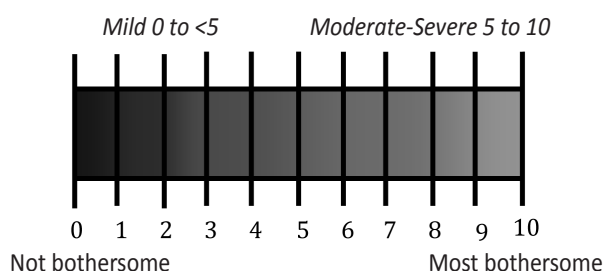
*Grade A Recommendation, Level 1C Evidence*

Gendo et al (2004) showed that eliciting the following points in the medical history would lead to an accurate diagnosis of AR: allergy triggers, presence of nasal symptoms and watery-itchy eyes, positive personal history of atopy, and positive family history of atopy (positive likelihood ratios ranging from 2.49 to 6.69).<sup>(5)</sup> Crobach et al (1998) earlier showed that medical history alone compared favorably to radioallergosorbent tests (RAST) and skin prick tests (SPT) for allergies to tree pollen, grass pollen, weed pollen, house dust mite, mold, cat dander, and dog dander. When only the medical history was used, the diagnostic power of the logistic regression model was 0.77 to 0.89.<sup>(6)</sup>

Supportive clinical information that must be sought includes the following:

- 1.1 The frequency and duration (intermittent or persistent) and severity of symptoms
- 1.2 Personal history of other manifestations of atopy
- 1.3 Family history of atopy
- 1.4 Identification of possible allergens in the environment: home, workplace, school, etc.
- 1.5 Absence of symptoms upon change of environment
- 1.6 Result of previous allergy testing (e.g., skin test, serum specific IgE test, nasal provocation test)
- 1.7 The effects of previous allergen avoidance measures

Figure 1. Visual Analog Scale (VAS)



The severity of the disease may be evaluated using a visual analog scale in answer to the question of “*how bothersome are your symptoms of rhinitis?*” This can help guide the clinician on the appropriate management.<sup>(7)</sup>

- 1.8 Response to pharmacological treatment and previous immunotherapy
- 1.9 A simple Visual Analog Scale (VAS) quantifying the severity of rhinitis symptoms (Figure 1)

**2. Anterior rhinoscopy must be performed to support the diagnosis of AR and other nasal pathology. The following findings may be observed:**

- 2.1 Pale gray, dull red, or red turbinates
- 2.2 Boggy turbinates
- 2.3 Minimal to profuse, watery to mucoid nasal discharge

*Grade D Recommendation, Level 5 Evidence*

Anterior rhinoscopy using a nasal speculum and head mirror/head light, although offering a limited view, remains an appropriate method for studying pathologic signs observed in most cases of allergic rhinitis. Moreover, anterior rhinoscopy helps to exclude conditions other than AR (e.g., nasal polyposis, infectious rhinitis, nasal septal deviation, sinonasal tumors and systemic disorders with sinonasal manifestations).<sup>(1, 3)</sup>

Examination is performed before and after topical decongestion and, when needed, topical anesthesia. Suctioning of excessive secretions is also performed to optimize visualization.

The diagnosis of AR based on physical examination (PE) alone is not reliable and consistent. Raza et al (2011) found that PE alone has a Sensitivity (SN) of 67%, Specificity (SP) of 63%, Positive predictive value

(PPV) of 50%, and a Negative predictive value (NPV) of 80%. This may be due to relative subjectivity in evaluating the nasal cavity. However, combining history with PE increases the diagnostic accuracy to SN=87%, SP=87%, PPV=77%, and NPV=93%.<sup>(8)</sup>

**3. Nasal endoscopy is strongly recommended for selected patients.**

*Grade A Recommendation, Level 1C Evidence*

Nasal endoscopy allows a more thorough visualization of nasal and nasopharyngeal structures with a sensitivity of 84% and a specificity of 92%. Endoscopy was found to identify more disease than rhinoscopy (85% versus 74%); and a similar picture was seen when combining history with either endoscopy or rhinoscopy. It provides valuable information especially in cases with atypical symptoms, complications, treatment failures, or when other pathology is suspected.<sup>(9, 10)</sup>

**4. A complete Ear, Nose and Throat (ENT) examination must be performed on all patients with AR.**

*Grade D Recommendation, Level 5 Evidence*

Performing a complete ENT examination provides information on the chronicity and severity of the patient’s AR (e.g., high-arched palate, open-mouth posture, Denny-Morgan lines, nasal crease). The presence of other associated conditions, such as otitis media with effusion, may also be uncovered.

**5. Detailed allergic work-up, e.g., skin tests, serum specific IgE tests, or nasal provocation tests, may be performed for the following:**

- 5.1 Patients with whom a questionable diagnosis exists
- 5.2 Patients unresponsive or intolerant to pharmacotherapy
- 5.3 Patients with multiple target organ involvement (i.e., allergic manifestations in the eyes, nose, throat, skin, lungs, etc.)
- 5.4 Patients for whom immunotherapy is considered
- 5.5 Patients with suspected Local AR (LAR)\*

*Grade A Recommendation, Level 1C Evidence*

Specific IgE testing is indicated to provide evidence of an allergic basis for the patient’s symptoms, to confirm or exclude suspected causes of the patient’s symptoms, or to assess sensitivity to specific allergens for avoidance measures and/or allergen immunotherapy.<sup>(6, 11, 12)</sup>

In general practice, if skin tests are not readily available, serum specific IgE tests may be carried out. With the advent of Molecular Allergy, the standardization and number of tested allergens is expected to increase and skin testing may eventually be replaced by tests such as ImmunoCAP Immune Solid-phase Allergy Chip (ISAC).<sup>(13, 14)</sup>

Cost and geographic constraints were considered by the panel as important clinical modulating factors in our setting. Benefits of allergy testing include high accuracy and low adverse effects. However, these tests are relatively expensive and may not be readily accessible to many patients.

\***Local allergic rhinitis (LAR)** is a subset of AR wherein patients have a clinical history and physical examination findings consistent with AR, but have no evidence of systemic atopy (i.e., negative skin prick tests, negative serum specific IgE tests). However, on nasal provocation testing



with aeroallergens, patients with LAR show local increased levels of specific IgE, tryptase, and eosinophilic cationic protein (ECP). Rondon et al (2012), found a 28.9% prevalence of LAR in patients with AR. LAR is treated as AR.<sup>(15)</sup>

**RECOMMENDATIONS ON THE TREATMENT OF ALLERGIC RHINITIS IN ADULTS**

**1. Patients should be advised to avoid or minimize exposure to allergens.**

**1.1 Highly pollen-allergic individuals should limit exposure to the outdoors when high pollen counts are present.**

*Grade B Recommendation, Level 2C*

Cua-Lim (1978) identified grass pollen as the predominant pollen in the Philippines, followed by Mimosa, Moraceae, Cyperaceae, lower vascular plants spores, Amaranth, Coconut, Tiliaceae, Pinus, Compositae and Alnus.<sup>(16)</sup> Regionally, Andiappan et al (2014) found that Bermuda grass, Common ragweed, and Acacia were the predominant outdoor allergens in Singapore.<sup>(17)</sup> Bunnag et al (2009) reported that Bermuda grass, para grass, sedge, careless weed were the predominant outdoor allergens in Thailand.<sup>(18)</sup>

Weather factors affect pollen counts in various ways. High humidity, moisture and barometric pressure cause pollen to rupture into tiny particles that can be carried and distributed by winds. Pollen counts are generally highest on sunny, windy days with low humidity.<sup>(1, 19-21)</sup>

Limiting exposure to the outdoors may include exercising indoors, keeping doors and windows closed, doing activity after 10 a.m. (when pollen counts are lower), wiping pets that have come in from outside with a damp cloth to remove pollen on their coats, and washing and drying clothes indoors to avoid pollen contamination.

**1.2 Indoor allergen avoidance may provide some benefit for patients with AR.**

**1.2.1 Clinically effective dust mite avoidance includes a combination of measures such as humidity control, frequent change of beddings, avoidance of carpeting and heavy curtains, avoidance of clothed upholstery, dust mite covers for beddings, and the use of tea sprays or acaricides.**

**1.2.2 Reduction of indoor fungal exposure involves removal of moisture sources, replacement of contaminated materials, and the use of dilute bleach solutions on nonporous surfaces.**

**1.2.3 Removal is the most effective way to manage animal or cockroach sensitivity.**

**1.2.4 Pollen movement indoors may be minimized by closure of doors and windows during the relevant time of year, and by active removal from indoor air through the use of high-efficiency particulate air filters.**

*Grade B Recommendation, Level 2B Evidence*

In the Philippines, Cua-Lim (1994) found that the most common aeroallergens were house dust mites (87%), cockroach (41%), mold spores (37%), cat dander (36%), kapok (35%), dog dander (32%), grass pollens (26%), weed pollens (25%), Acacia pollen (2%).<sup>(22)</sup>

In Fullante and Hernandez' (2005) unpublished observations, they found that the most common indoor allergens are house dust mite (69.3%), cockroach (56.8%), and cat hair (8%).<sup>(23)</sup> In a recent study of children with AR, Santos-Reyes and Gonzalez-Andaya (2014) found that *D. farinae* (86%), *D. pteronyssinus* (87%), *B. tropicalis* (60%), cat pelt (47%), and cockroach (45%) were the most predominant allergens.<sup>(24)</sup> Regionally, Andiappan et al (2014) found that *Blomia tropicalis* (68.9%), *Dermatophagoides pteronyssinus* (68.5%), and German cockroach (14.6%) were the predominant indoor allergens in Singapore.<sup>(17)</sup> Bunnag et al (2009) reported that house dust mite (64.7%), cockroach (49.8%), and dog (44.2%) were the predominant indoor allergens in Thailand.<sup>(18)</sup> Asha'ari et al (2010) found that house dust mite (80%), cat dander (37.8%), and *Mucor mucedo* (20%) were the predominant indoor allergens in Malaysia.<sup>(25)</sup>

Indoor allergen avoidance measures have been shown to reduce allergen levels but do not necessarily result in symptom control or decreased medication use.<sup>(1, 19, 26-33)</sup>

**1.3 Multimodal environmental control strategies are better than any single strategy.**

*Grade D Recommendation, Level 5 Evidence*

Individual allergen avoidance measures have failed to show consistent decrease in AR symptoms and/or medication use. Combining environmental control strategies may offer more benefit for patients with AR.<sup>(1, 2, 19)</sup> When the quality of life (QOL) is severely affected due to allergen exposure, transfer of residence/work may be considered.

**2. Nasal saline irrigation (NSI) or douching is recommended as an adjunctive treatment for patients with allergic rhinitis.**

*Grade A Recommendation, Level 1A– Evidence*

A meta-analysis done by Hermelingmeier (2012) showed NSI performed regularly was observed to have a positive effect on all investigated outcome parameters in adults and children with AR. NSI produced a 27.66% improvement in nasal symptoms, a 62.1% reduction in medicine consumption, a 31.19% acceleration of mucociliary clearance time, and a 27.88% improvement in quality of life.<sup>(34)</sup>

Studies on NSI are heterogeneous as to the type, amount, and timing of nasal irrigation and the use of different saline solutions. Nevertheless, NSI is well tolerated, inexpensive, easy to use, and there is no evidence showing that regular, daily irrigation adversely affects the patient's health or causes unexpected side effects.<sup>(34)</sup>

**3. Oral antihistamines are strongly recommended in AR with intermittent symptoms and short term allergen exposure.**

**3.1 Oral antihistamines have been found to cause statistically significant improvement of nasal symptoms in patients with allergic rhinitis.**

*Grade A Recommendation, Level 1A Evidence*

Oral antihistamines have a rapid onset of action, once-daily dosing, maintenance of effectiveness with regular use, and the availability of some drugs over the counter without need of a prescription. Some patients who

fail to improve with one agent may respond to an alternative drug in this category. Maximum benefit is seen with continuous use, but use on an as-needed basis can provide significant symptom relief and is appropriate for some patients, especially those with intermittent symptoms.<sup>(1-3, 35)</sup>

**3.2 Second-generation antihistamines are generally preferred over first-generation antihistamines because the former are associated with less sedation, performance impairment, and anticholinergic effects.**

*Grade B Recommendation, Level 2B Evidence*

Histamine in the brain facilitates learning and memory, and regulates the circadian sleep/wake cycle. First-generation antihistamines, which cross the blood-brain barrier, interfere with histamine's functions. Moreover, the long half-lives of drugs (≈24 hours) such as diphenhydramine, chlorpheniramine and hydroxyzine, mean that these effects are still present the following morning leading to daytime somnolence, increased traffic accidents, decreased productivity at work and reduced children's learning. Second-generation H1 antihistamines are largely devoid of these effects.<sup>(1-3, 36)</sup>

**4. Intranasal antihistamines are recommended alternative therapy to oral antihistamines in AR with intermittent symptoms and short term exposure to allergens.**

*Grade A Recommendation, Level 1A Evidence*

Intranasal antihistamines are efficacious and equal or superior to oral second-generation antihistamines. Antihistamines are generally less effective than intranasal corticosteroids.<sup>(1, 37-39)</sup>

**5. Intranasal corticosteroids (INCS) for at least one month, is strongly recommended in AR with intermittent moderate-severe symptoms, persistent symptoms, and long-term exposure to allergens. Duration of therapy can be individualized based on patient follow-up findings.**

*Grade A Recommendation, Level 1A Evidence*

INCS are the most effective medication class in controlling symptoms of allergic rhinitis.<sup>(1, 2, 40)</sup>

**5.1 Topical antihistamines may be added to INCS for patients with inadequate control and exacerbation of symptoms.**

*Grade A Recommendation, Level 1B Evidence*

Studies have shown that the combination of INCS and topical antihistamines is more effective than INS and topical antihistamine monotherapy.<sup>(1-3, 41)</sup>

**5.2 Oral antihistamines may be considered when topical antihistamines are unavailable.**

*Grade D Recommendation, Level 5 Evidence*

Due to scarcity of topical antihistamine in the local setting, the addition of oral antihistamine in combination with INCS for cases with uncontrolled AR symptoms or in cases of exacerbation is an option.

**6. A short course of oral corticosteroids (5 to 7 days) may be recommended in AR with moderate-severe and persistent symptoms not responsive to INCS.**

*Grade B Recommendation, Level 2C Evidence*

Short course systemic corticosteroids are often used clinically for patients with severe AR but this lacks evidence of superiority to INCS. A paper by Karaki et al (2013) comparing the use of INCS versus systemic corticosteroid revealed no significant difference making INCS sufficient in the treatment of AR.<sup>(42)</sup> Also, due to known side effects, oral corticosteroids are not routinely given hence should not be considered as first-line treatment of AR patients.<sup>(1-3, 42)</sup>

**7. Oral anti-leukotriene agents, alone, in combination with antihistamines, or in combination with INCS, may be recommended in AR especially in the presence of asthma.**

*Grade A Recommendation, Level 1A Evidence*

Recognizing that as many as 40% of patients with AR have coexisting asthma, montelukast may be considered when treatment can benefit both upper and lower airways.<sup>(1-3, 43-45)</sup>

**8. Intranasal cromolyn sodium may be used in AR, especially because of its lesser side effects. However, it is less effective than corticosteroids, and has not been adequately studied in comparison to anti-leukotriene and antihistamine agents.**

*Grade A Recommendation, Level 1B Evidence*

Cromolyn sodium inhibits the degranulation of sensitized mast cells, thereby blocking the release of inflammatory and allergic mediators. It may be given several hours prior to allergen exposure, thus preventing symptoms of the early phase reaction. However, adherence is poor because it should be taken 4 times daily compared to once or twice daily dosing for antihistamines and INCS.<sup>(1, 2, 46)</sup>

Chromones are safe, even for small children and pregnant women, however, they are less efficacious compared to antihistamines, and are not strongly recommended as first line treatment of AR.<sup>(1, 2, 46, 47)</sup>

**9. Oral and topical decongestants may be used for patients with prominent nasal obstruction. However, they must be used judiciously and according to pharmacologic indications.**

**9.1 Oral decongestants can reduce nasal decongestion but can result in side effects such as insomnia, irritability and palpitations.**

*Grade A Recommendation, Level 1B Evidence*

Oral decongestants have clearly shown improvement of nasal obstruction and are even more efficacious if given together with INCS.<sup>(48)</sup> However, due to possible adverse effects of headache, dry mouth, hypertension, and nervousness, use of decongestants is limited to short course treatment.<sup>(1, 2)</sup>

**9.2 Topical decongestants can be considered for short-term or possibly intermittent or episodic therapy of nasal congestion, but are inappropriate for long-term daily use because of the risk for the development of rhinitis medicamentosa.**

*Grade B Recommendation, Level 2B*

Development of rhinitis medicamentosa poses a significant concern for clinicians prescribing topical decongestants. While topical decongestants are often given for 3-10 days, there is insufficient literature on the appropriate duration of use.<sup>(1-3, 46)</sup> Toohill et al (1981) found a 1% incidence of rhinitis medicamentosa in his practice.<sup>(49)</sup>

**9.3 Oral and topical decongestants should be used with caution in patients of any age who have a history of cardiac arrhythmia, angina pectoris, cerebrovascular disease, hypertension, bladder neck obstruction, glaucoma or hyperthyroidism.**

*Grade B Recommendation, Level 2A– Evidence*

Regular use of oral and topical decongestants comes with caution so as to avoid adverse effects particularly involving the cardiovascular and neurovascular systems. A meta-analysis study by Salerno et al (2005) concluded “pseudoephedrine caused a small but significant increase in systolic blood pressure (0.99 mm Hg; 95% CI, 0.08 to 1.90) and heart rate (2.83 beats/min; 95% CI, 2.0 to 3.6) with no effect on diastolic blood pressure (0.63 mm Hg, 95% CI, -0.10 to 1.35)”.<sup>(50)</sup> Decongestants may be given as rescue medication to patients with inadequate response to INCS and antihistamines and/or in cases of symptom exacerbation.<sup>(1-3, 51)</sup>

**10. Combination preparations of pharmacotherapeutic agents may be considered for patients suffering from AR with inadequate response to monotherapy.**

*Grade D Recommendation, Level 5 Evidence*

Formulations combining two drugs such as oral antihistamine and oral decongestant, oral antihistamine and oral montelukast, oral antihistamine and oral steroid, topical antihistamine and INCS may offer additional symptom relief for some patients, as well as the convenience of single intake dosing.<sup>(1, 2)</sup>

**11. Allergen specific immunotherapy (SIT) is effective for the treatment of AR.**

**11.1 Allergen immunotherapy may prevent the development of new allergen sensitizations and reduce the risk for the future development of asthma in patients with AR.**

*Grade A Recommendation, Level 1A Evidence*

SIT represents the only treatment that can alter the natural history of AR. It restores normal immunity and/or increases tolerance against allergens resulting in decreased AR symptoms, and long-term allergen-specific immune tolerance. Overall, available evidence supports the effectiveness and safety of both subcutaneous and sublingual immunotherapy for the treatment of allergic rhinitis.<sup>(1, 2, 46, 52-55)</sup>

**11.2 It may be used in the following select group of AR patients:**

- Patients who did not benefit from avoidance therapy and pharmacotherapy

- Patients who cannot tolerate or who refuse pharmacotherapy
- Patients who are chronically exposed to allergens
- Patients with rhinitis and symptoms from the lower airways during peak allergen exposure

*Grade A Recommendation, Level 1B Evidence*

Immunotherapy produces significant improvement of AR symptoms which leads to improvement of quality of life and decreased need for medical therapy. The positive benefit of SIT continues even after discontinuation. A study by Jacobson et al (2007) documented that beneficial effects were observed at 10 and 8 years after treatment cessation for subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), respectively.<sup>(56)</sup>

Additional advantages of SIT are prevention of asthma and reduction of new sensitizations.<sup>(1, 2, 52, 56, 57)</sup>

**11.3 The use of SIT has potential adverse effects. These are classified as local (SCIT: redness and induration at site of injection; SLIT: oral itching and discomfort) or systemic reactions (urticaria, gastrointestinal upset, wheezing and anaphylaxis). Thus, SIT should not be used in patients with uncontrolled asthma.**

*Grade B recommendation, Level 2B Evidence*

A safety data systematic review of SIT by Lin et al (2003) reported rates of local reactions ranging from 0.6% to 58% for SCIT and 0.2% to 97% for SLIT.<sup>(1, 53)</sup>

The rate of systemic reactions has been reported to be from 0.6% to 0.9% and deaths at 1 per 2.5 million (3.4 deaths per year) for SCIT.<sup>(58, 59)</sup> No deaths were recorded for SLIT.<sup>(1)</sup>

Due to possibility of serious adverse effects, it is recommended that SCIT should not be used in patients with uncontrolled asthma. Additionally, SCIT should be administered in a clinic where serious reactions can be promptly recognized. Patients should also be observed for 30 minutes after injection.<sup>(59)</sup>

**11.4 Patients must be well-informed of the costs of SIT before initiating it.**

*Grade D recommendation, Level 5 Evidence*

The cost of immunotherapy in the Philippine General Hospital Allergy Section is 90-280 pesos for charity patients, and 190-390 pesos for private patients per injection of allergens (Espiritu AMV 2015, oral communication, 1st October). In private hospitals (Abong JM 2015, oral communication, 1st October), rates vary widely. The initial injection is at least 700 pesos and the cost goes up as the concentration of the allergen in solution increases with subsequent injections. Charity patients spend approximately 800-1,600 pesos/month, while private patients may pay upwards of 2,800 pesos/month.<sup>(60, 61)</sup>

**12. VAS scoring should be done periodically to assess symptom severity, and monitor response to treatment.**

*Grade A Recommendation, Level 1C Evidence*

Bousquet et al (2007) concluded that a simple and quantitative method (VAS) can be used for the evaluation of the severity of allergic rhinitis. In this study, the receiver operating characteristic curve results showed that patients with a VAS of under 5 cm could be classified as ‘mild’ rhinitis (negative predictive value: 93.5%) and those with a VAS of over 6 cm as ‘moderate/severe’ rhinitis (positive predictive value: 73.6%).<sup>(7)</sup>

**13. A multidisciplinary approach to treatment, including referrals to other specialists, may be necessary for selected patients, especially those with uncontrolled AR.**

*Grade D Recommendation, Level 5 Evidence*

Bousquet et al (2010) determined that about 20% of patients being treated for AR had uncontrolled symptoms, and that these patients had a VAS of 5 or more.<sup>(62)</sup> Hence, **Uncontrolled AR** is defined as patients with AR having persistent symptoms with a severity of VAS > 5, despite pharmacologic treatment and allergen avoidance.

Hellings et al (2013) suggested that patients with uncontrolled AR be investigated for disease-related, diagnosis-related, treatment-related, and patient-related factors that may contribute to the persistent symptoms of AR.<sup>(63)</sup> Disease-related factors may include allergen load, cigarette smoke, pollutants, occupational factors, hormonal factors, genetic factors, and even innate steroid resistance. Diagnosis-related factors may include missing the presence of nasal hyperreactivity, septal deviation, nasal valve dysfunction, nasal polyps, adenoidal hypertrophy, or even a CSF leak. Patient-related factors may include inappropriate use of intranasal sprays and wrong technique and positioning. Patient perceptions about his condition, and expectations with treatment may also impact adherence to therapy. Treatment-related factors include inappropriate route and dose of drug administration, and treatment modality that is inappropriate for the patient’s symptom severity.<sup>(63)</sup>

Patients with persistent AR with possible asthma, patients with multiple target organ involvement, and those with failure of medical treatment will benefit from consultations with other specialties.<sup>(1-3)</sup>

**14. Although there is no surgical treatment for allergic rhinitis, surgery may be indicated in the management of comorbid conditions.**

*Grade C Recommendation, Level 2B Evidence*

Indications for a surgical intervention include the following:<sup>(1, 19)</sup>

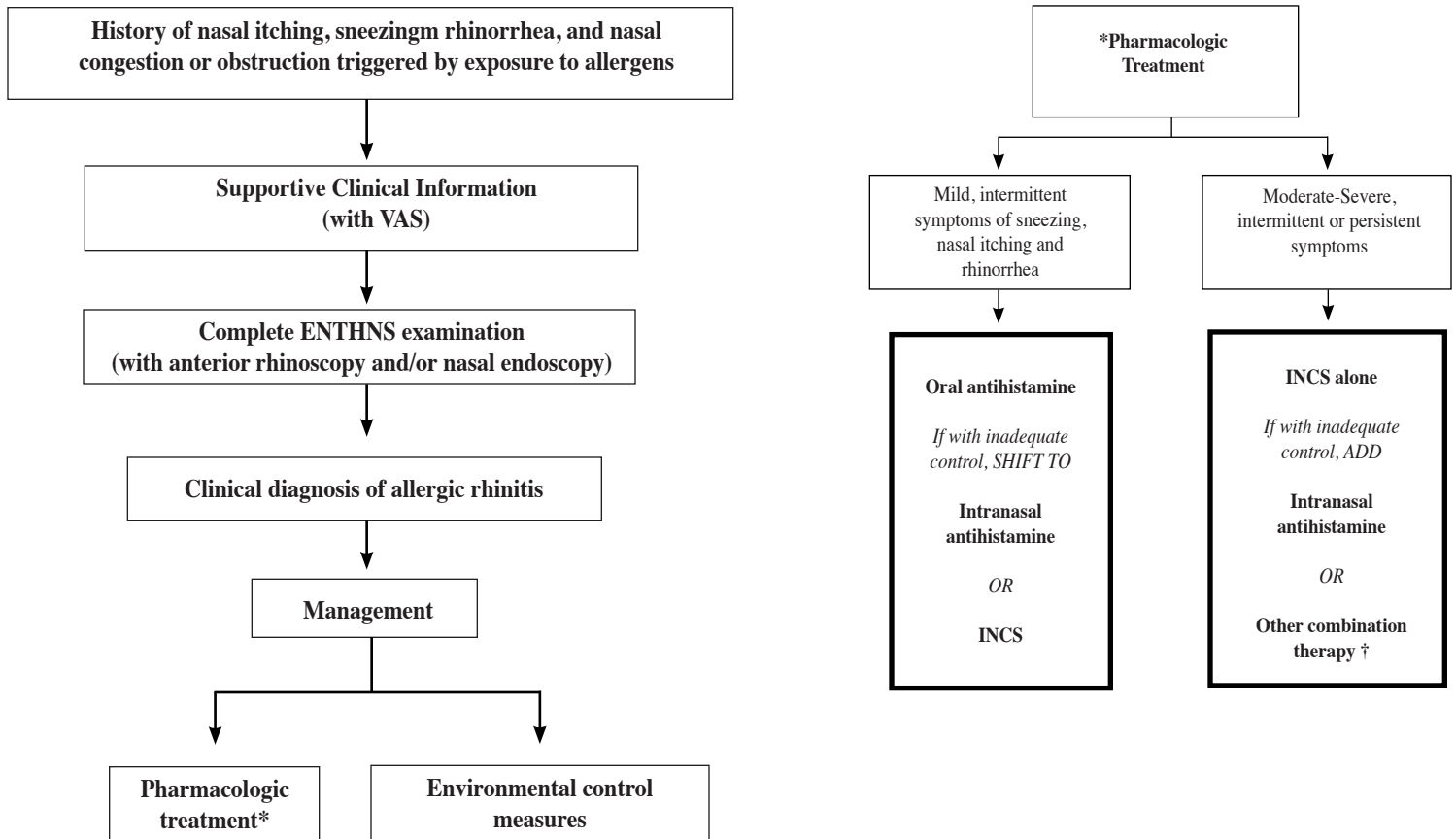
- Inferior turbinate hypertrophy unresponsive to medications<sup>(64)</sup>
- Anatomical variations of the septum with functional relevance
- Adenoidal hyperplasia
- Anatomical variations of the bony pyramid with functional relevance
- Secondary or independently developing chronic rhinosinusitis and complications thereof

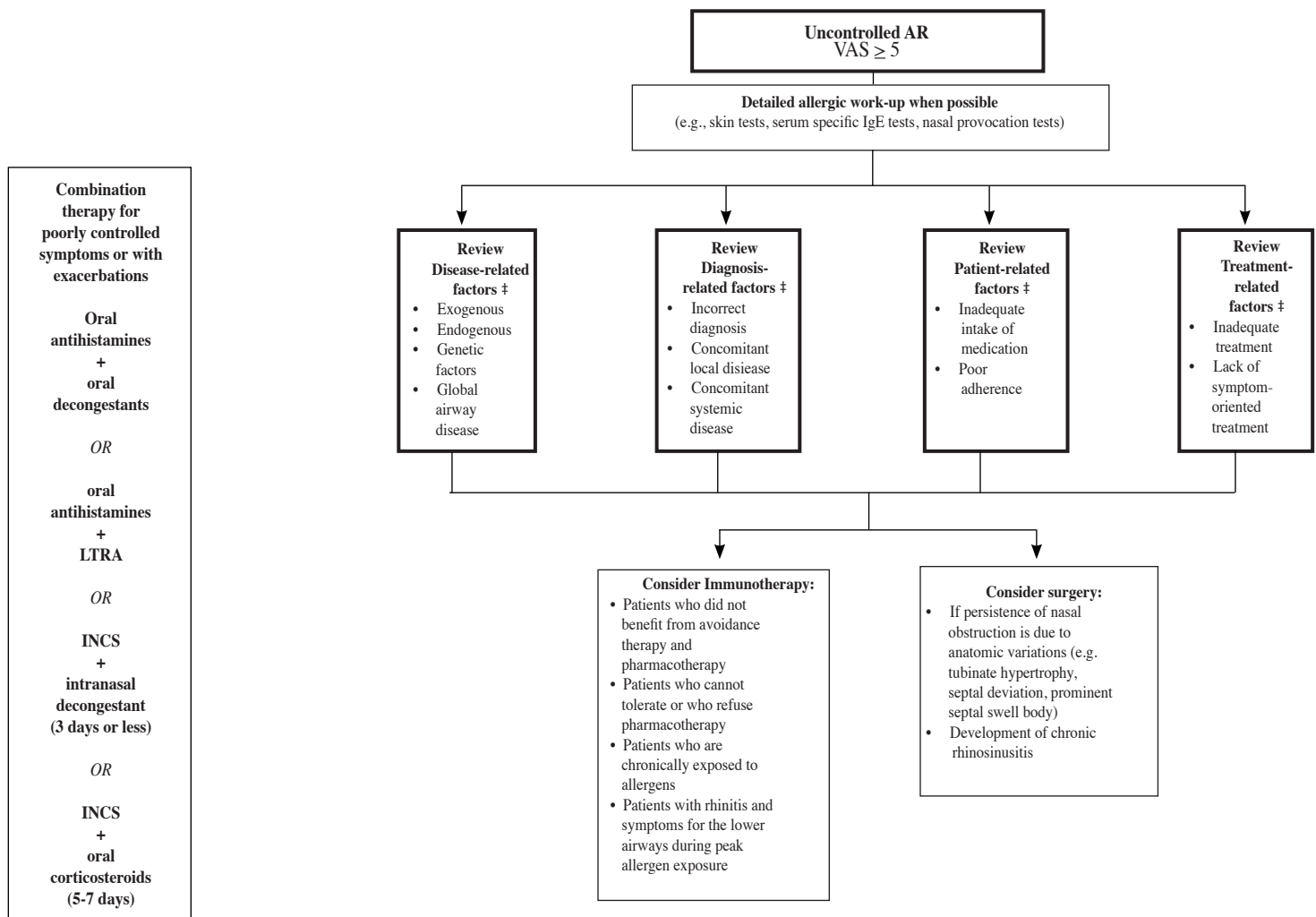
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### DIAGNOSIS AND TREATMENT FLOWCHART FOR ALLERGIC RHINITIS IN ADULTS





‡Adapted from Hellings et al (2013) <sup>(63)</sup>

# ACUTE BACTERIAL RHINOSINUSITIS IN ADULTS

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## PURPOSE

This clinical practice guideline (CPG) is intended to describe appropriate care based on the best available scientific evidence and broad consensus for acute bacterial rhinosinusitis in adults. It aims to reduce inappropriate variations in clinical practice and to highlight management principles unique to the specialty of Otorhinolaryngology in the Philippines.

## TARGET POPULATION, SETTING AND PROVIDERS OF CARE

This CPG is for use by the Philippine Society of Otolaryngology-Head and Neck Surgery. It covers the diagnosis and management of Acute Bacterial Rhinosinusitis (ABRS) in adults.

## OBJECTIVES

The objectives of this guideline are (1) to provide the requisite criteria for the diagnosis of acute bacterial rhinosinusitis; (2) to describe the current diagnostic techniques; and (3) to recommend management options relevant to the local setting.

## METHODOLOGY

The panel was asked to review the previously published PSO-HNS CPG for Acute Bacterial Rhinosinusitis in Adults. Data from scientific studies were presented in an analytical framework in the initial panel meeting, and revisions and recommendations were formulated. In the present document, an extensive MEDLINE, National Library of Medicine's PubMed database, and Agency for Healthcare Research and Quality (AHRQ) Evidence Report and Technology Assessment was done using the keyword "acute sinusitis" or "acute rhinosinusitis"; exploded to include the *definition/classification, prevalence/epidemiology, diagnosis, and therapy*. The search was limited to articles involving adult (19 years old and above) humans, and those published in English from 2006 to 2015. The search yielded 310 articles, which included the following:

Meta-analysis/Systematic Reviews:	27
Randomized controlled trial:	64
Consensus report/ CPG:	2

Additionally, older relevant literatures were included. A draft of the evidence-based recommendations (EBR) was collated and presented by the panel to the general assembly of ENT-HNS specialists.

This guideline will undergo review and updating five (5) years after publication, or earlier, depending on the availability of new information.

## FUNDING AND DISCLAIMER

The development of this guideline was funded exclusively by the Philippine Society of Otolaryngology-Head and Neck Surgery. The views or interests of the funding body have not influenced the final recommendations.

## COMPETING INTERESTS

All authors have declared that they have no competing interests.

## DEFINITION

**Rhinosinusitis** is a group of disorders characterized by inflammation of the mucosa of the nose and paranasal sinuses.<sup>(1)</sup> Sinusitis is generally preceded by rhinitis and rarely occurs without concurrent rhinitis, therefore, sinusitis is best described as rhinosinusitis.<sup>(2)</sup>

**Acute rhinosinusitis (ARS)** is an inflammatory condition involving the paranasal sinuses, as well as the lining of the nasal passages, which lasts up to 4 weeks (28 days).<sup>(1)</sup> In general, a diagnosis of **acute bacterial rhinosinusitis (ABRS)** may be made in adults with symptoms of a viral upper respiratory infection (URI) that have not improved after 10 days or worsen after 5 to 10 days.<sup>(2)</sup> There may be some or all of the following symptoms: nasal drainage, nasal congestion, facial pressure/pain, postnasal drainage, hyposmia/anosmia, fever, cough, fatigue, maxillary dental pain, and ear pressure/fullness.<sup>(2)</sup> On the other hand, the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) has included all cases lasting for < 12 weeks with complete resolution of symptoms under acute rhinosinusitis.<sup>(3)</sup>

The most common bacterial species isolated from the maxillary sinuses in adults with ABRS are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.<sup>(2)</sup> Other streptococcal species, anaerobic bacteria, and *Staphylococcus aureus* have also been documented in a smaller percentage of cases.

## PREVALENCE

The prevalence of bacterial infection in patients with diagnosed ARS is not well-defined given the difficulty of distinguishing viral from bacterial ARS because the clinical features are similar.<sup>(2,4)</sup> Predisposing factors for rhinosinusitis include allergic rhinitis, non-allergic rhinitis, nasal polyps, rhinitis medicamentosa, trauma, dental infections, immunodeficiency, or other factors that lead to inflammation of the nose and paranasal sinuses. In addition, rhinosinusitis is found more commonly in patients with tumors, Wegener's granulomatosis, HIV infection, Kartagener's syndrome, immotile cilia syndrome, and cystic fibrosis.<sup>(2)</sup>

Presumed bacterial ARS (ABRS) is one of the most common conditions encountered by clinicians. Secondary bacterial infection of the paranasal sinuses following an antecedent viral upper respiratory tract infection (URI) is estimated to be 0.5% - 2% of adult cases.<sup>(1)</sup> The prevalence of a bacterial infection during ARS is estimated to be 2% - 10%, whereas viral causes account for 90% - 98%. Several imaging, clinical and laboratory tests have been used to increase the likelihood of a correct diagnosis of ABRS with endoscopically directed middle meatal cultures (EMMC)



being a viable culture method for determining antimicrobial efficacy and bacterial resistance patterns.<sup>(5, 6)</sup>

**RECOMMENDATIONS ON THE DIAGNOSIS OF ACUTE BACTERIAL RHINOSINUSITIS (ABRS)**

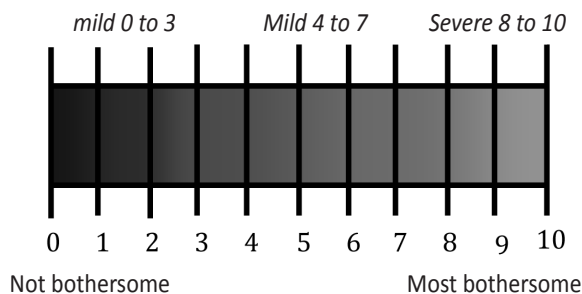
1. **The diagnosis of ABRS is based on the following criteria:**
  - **Acute onset of some or all of the following symptoms: nasal congestion, purulent nasal discharge (anterior/posterior nasal drip) with or without facial pain/pressure, dental pain and ear pressure/fullness, fever, cough, fatigue, hyposmia/anosmia that fail to improve after 10 days**
  - **Symptoms worsening within 5-10 days after an initial improvement (i.e. double worsening)**
  - **Symptoms not lasting beyond 4 weeks**

*Grade D Recommendation, Level 5 Evidence*

In the first 3 to 4 days of illness, there is difficulty in differentiating a viral etiology from early-onset bacterial etiology of rhinosinusitis. If symptoms persist for 5 to 10 days, this could represent the beginning stages of ABRS. In this time period, a pattern of initial improvement followed by worsening characterized by new onset of fever, headache or increased nasal discharge may be observed. This pattern of “double worsening” or “double sickening” is consistent with ABRS.<sup>(1, 2, 7)</sup>

The severity of the disease may be evaluated using a visual analog scale (Figure 1) in answer to the question of “how troublesome are your symptoms of rhinosinusitis”? This can help guide the clinician on the appropriate management.<sup>(1)</sup>

Figure 1: Visual Analog Scale (VAS)



2. **A thorough physical examination should include inspection, palpation of the maxillary and frontal sinus, as well as anterior and posterior rhinoscopy.**

*Grade D recommendation, Level 5 Evidence*

Performing a complete ENT examination provides information on the chronicity and severity of the patient’s ABRS. The presence of other associated conditions, such as otitis media with effusion, may also be uncovered. Nasal decongestion and suctioning of excess secretions may be performed to aid in diagnosis.

3. **Nasal endoscopy is a safe, radiation-free, and relatively inexpensive office procedure. It may be used to examine the nasal cavity and**

**nasopharynx for anatomical abnormalities and the origin of purulent discharge. Additionally, endoscopy-guided retrieval of samples for microbiological culture may be done.**

*Grade C Recommendation, Level 4 Evidence*

In a prospective controlled study by Berger and Berger regarding the use of flexible endoscopy for diagnosis of ABRS, it was shown that using clinical criteria alone had moderate predictive value of 66.3%, highlighting the need for objective measures for diagnosis of ABRS.<sup>(6)</sup>

Endoscopically guided cultures of the discharge from the middle meatus have a sensitivity of 81%, specificity of 91%, positive predictive value of 83% and negative predictive value of 89%, with an overall accuracy of 87% compared with direct sinus aspiration.<sup>(5)</sup> It may be performed in selected cases: 1] in the establishment of present local bacteriology and resistance; 2] in cases where initial antibiotics fail to improve patient symptoms; 3] or in patients with immune-compromised status or with severe infection.<sup>(5)</sup>

4. **Imaging Studies are NOT recommended for the routine diagnosis of ABRS.**

*Grade A(-) Recommendation, Level 1A Evidence*

Sinus radiography has moderate sensitivity (76%) and specificity (79%) compared with sinus puncture in diagnosing ABRS. Sinus involvement is common in documented viral URIs, making it impossible to distinguish ABRS from viral ARS based solely on imaging studies. Plain films of the sinuses are inaccurate in a high percentage of patients.<sup>(8)</sup>

5. **Imaging Studies are reserved for patients with persistent symptoms, recurrent ABRS or complications, and when sinus surgery is contemplated.**

*Grade A(-) Recommendation, Level 1A Evidence*

When a complication of ABRS or an alternative diagnosis is suspected, imaging studies may be obtained.<sup>(8)</sup> Complications of ABRS may include orbital, intracranial, or soft tissue involvement while alternative diagnoses include malignancy and other noninfectious causes of facial pain. Radiographic imaging may also be obtained when the patient has co-morbidities that predispose to complications, including diabetes, an immune-compromised state, or a history of facial trauma or surgery.<sup>(7, 9)</sup>

CT imaging of the sinuses is appropriate when a complication of ABRS is suspected based on severe headache, facial swelling, cranial nerve palsies, or forward displacement or bulging of the eye (proptosis). The CT findings that correlate with ABRS include opacification, air-fluid level, and moderate to severe mucosal thickening.<sup>(7, 9, 10)</sup>

Complications of ABRS are best assessed using iodine contrast-enhanced CT or gadolinium-based Magnetic Resonance Imaging (MRI) to identify extra-sinus extension or involvement. Suspected complications are the only indication for MRI of the Paranasal sinuses in the setting of ABRS.<sup>(7, 9, 11)</sup>

**RECOMMENDATIONS ON THE TREATMENT OF ACUTE BACTERIAL RHINOSINUSITIS**

**1. The primary treatment for Acute Bacterial Rhinosinusitis (ABRS) is empiric antibiotic therapy.**

*Grade A Recommendation, Level 1A and 2B Evidence*

- 1.1 First-line antimicrobial regimen for ABRS in patients with low-risk for antimicrobial resistance:

Amoxicillin-Clavulanic Acid 625mg q8h or 1g q12h OR  
Amoxicillin alone at 500mg q8h or 1g q12h

Patients at low risk for antimicrobial resistance are those <65 years of age, no prior antibiotic use within the past 30 days, no prior hospitalization in the past 5 days, no co-morbidities and not immunocompromised.<sup>(12)</sup>

Amoxicillin may still be used for patients with no history of antibiotic use in the past 6 weeks and where local resistance patterns support its use.<sup>(1, 12)</sup>

- 1.2 Seven (7) to ten (10) days is the recommended treatment duration for ABRS<sup>(7, 12-14)</sup>

- 1.3 For Penicillin allergy:  
Doxycycline 100mg q12h OR  
Levofloxacin 500mg OD OR  
Moxifloxacin 400mg OD

Respiratory Fluoroquinolones (Levofloxacin, Moxifloxacin) are not first line treatment and should only be used in penicillin-allergic patients.<sup>(15)</sup>

In recently published international guidelines, macrolides are not recommended as first-line therapy in ABRS due to increasing prevalence of *S. pneumoniae* resistance. However, local data on erythromycin for *S. pneumoniae* showed <5% resistance for the past decade.<sup>(16)</sup> Therefore, the use of macrolides may still be considered.

Second-generation cephalosporins are no longer recommended as monotherapy due to variable resistance patterns among *S. pneumoniae*.<sup>(12)</sup> However, due to absence of local data, the panel still considers this as an option in ABRS treatment.

**2. Second-line antimicrobial regimens are considered for patients at high risk of antimicrobial resistance and for failure of initial treatment.**

*Grade C Recommendation, Level 2B Evidence*

Failure of first-line treatment should be considered in all patients with worsening or no improvement of symptoms after 5-7 days and second-line antimicrobial regimen should be started.<sup>(7)</sup>

Second-line treatment options are the following:

- Amoxicillin-Clavulanic Acid 2g q 12h
- Doxycycline 100mg q 12h
- Levofloxacin 500mg OD
- Moxifloxacin 400mg OD

**3. Failure of second-line antibiotic treatment warrants further work-up.**

*Grade B Recommendation, Level 2B Evidence*

Patients with ABRS with inadequate response to treatment should be worked up for other conditions and possible disease modifiers.<sup>(5, 6, 9)</sup>

Further work-up may include, but not limited to, the following:

- 3.1 CT of the Paranasal Sinuses
- 3.2 Sinus or meatal culture
- 3.3 Immune system studies

**4. Watchful waiting is an option in uncomplicated ABRS (Temperature <38.3°C, no extra-sinus complications), provided that there is good follow-up.**

*Grade A Recommendation, Level 1A Evidence*

Early-onset viral ARS and ABRS show considerable overlap in inflammatory mechanisms and clinical presentation.<sup>(4, 7, 17)</sup> Antibiotic therapy is started if the patient's condition fails to improve 7 days after the diagnosis of ABRS has been made or if symptoms worsen at any time (double-worsening). Complications of ABRS are similar regardless of initial management.<sup>(7, 17)</sup>

**5. Nasal saline irrigation (NSI) is safe to use and is recommended as an adjunctive treatment.**

*Grade A Recommendation, Level 1A Evidence*

Hypertonic saline irrigation showed a modest benefit for ARS and may have superior anti-inflammatory effect and better ability to improve mucociliary clearance.<sup>(7, 18)</sup>

**6. Intranasal Corticosteroid Sprays (INCS) may be used as monotherapy or adjunct therapy to antibiotics in the empiric treatment of ABRS.**

*Grade A Recommendation, Level 1A Evidence*

Topical Nasal Steroids can be used alone or in combination with oral antibiotics for symptomatic relief of ABRS.<sup>(7, 19, 20)</sup>

A Cochrane review found that INCS increased the rate of symptom improvement from 66% to 73% after 15-21 days of use.<sup>(19, 20)</sup>

**7. There is a lack of available RCTs supporting the efficacy and use of topical and oral decongestants, and antihistamines in the treatment of ABRS.**

*Grade D Recommendation, Level 5 Evidence*

Symptomatic management should focus on hydration, analgesics, antipyretics, saline irrigation and INCS.<sup>(3, 7)</sup>

**8. In the management of patients with ABRS, patient education is important and should emphasize avoidance of inciting factors like allergens, environmental irritants or microbes (bacteria, fungi, virus), as well as discussing treatment options with emphasis on antibiotic resistance patterns.**

*Grade D Recommendation, Level 5 Evidence*

ABRS is frequently initiated by a viral upper respiratory infection. The pathophysiology in the development of ABRS involves an interplay between a predisposing condition (allergies, environmental irritants, anatomical deformities, and immune deficiency), infection and consequent inflammation of the nasal and paranasal sinus mucosa.<sup>(4)</sup>

Antimicrobial resistance is a global health problem. It causes prolonged illness, which may lead to mortality and risk of spreading the disease. It also creates a financial burden to the patient due to increased cost and prolonged duration of treatment. On the global economic scale, economic losses could be observed due to reduced productivity caused by the illness and higher cost of treatment. Thus, judicious use of antibiotics should be practiced and patients should be made aware of this by discouraging them from taking antibiotics without the advice of doctors.<sup>(21)</sup>

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# CHRONIC RHINOSINUSITIS IN ADULTS

Philippine Academy of Rhinology

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This guideline will undergo review and updating five (5) years after publication, or earlier, depending on the availability of new information.

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## COMPETING INTERESTS

All authors have stated that they have no competing interests.

## DEFINITION AND PREVALECE

**Rhinosinusitis** is a group of disorders characterized by inflammation of the mucosa of the nose and paranasal sinuses.

**Chronic rhinosinusitis (CRS)** is defined as inflammation of the nasal cavity and paranasal sinuses and/or the underlying bone that has been present for at least 12 weeks. It is primarily an inflammatory disorder due to multiple etiologic factors. There is increasing evidence that the recalcitrance and chronicity of this disease is due to a deranged host immune response against environmental agents.<sup>(1)</sup> Due to the obstruction of the sinuses secondary to the inflammatory process, there may be occasional acute exacerbations of rhinosinusitis associated with infection. However treating the infection, without addressing the underlying inflammatory disorder, will likely lead to increased frequency of exacerbations. Thus, accurate and comprehensive diagnosis and management is essential.

CRS is divided into two subgroups, **CRS without nasal polyps** (CRS w/o NP) and **CRS with nasal polyps** (CRS w/ NP). These have differences in etiopathogenesis and response to various treatment modalities.

**Nasal Polyps** are smooth, semi-translucent, pearly white to pinkish, pedunculated masses of edematous inflamed mucosa commonly originating from the ostiomeatal complex.

Surveys conducted in recent years using patient-reported symptoms of CRS lasting >12 weeks revealed a prevalence of 5-13% in the United States, Europe and China.<sup>(2)</sup> However, prevalence of doctor-diagnosed CRS is lower with rates of 2-4%.<sup>(3)</sup>

## RECOMMENDATIONS ON THE DIAGNOSIS OF CHRONIC RHINOSINUSITIS (CRS)

1. The diagnosis of CRS is based on the following criteria:
  - Presence of **two or more of the following symptoms, one of which should be either (a) nasal blockage/obstruction/congestion or (b) nasal discharge (anterior/posterior nasal drip); (c) facial pain/pressure; and (d) reduction or loss of smell.**
  - Duration of **≥12 weeks**
  - **AND presence of any of the following objective evidence of inflammatory disease, (a) mucopurulent discharge**

## PURPOSE

This clinical practice guideline (CPG) is intended to describe appropriate care based on the best available scientific evidence and broad consensus for chronic rhinosinusitis in adults. It aims to reduce inappropriate variations in clinical practice and to highlight management principles unique to the specialty of Otorhinolaryngology in the Philippines.

## TARGET POPULATION, SETTING AND PROVIDERS OF CARE

This CPG is for use by the Philippine Society of Otolaryngology-Head and Neck Surgery. It covers the diagnosis and management of Chronic Rhinosinusitis (CRS) in adults.

## OBJECTIVES

The objectives of the guideline are (1) to provide the requisite criteria for the diagnosis of CRS; (2) to describe current diagnostic techniques; and (3) to describe treatment options relevant to the local setting.

## METHODOLOGY

The panel was asked to review the previously published PSO-HNS CPG for Chronic Rhinosinusitis in Adults. Data from scientific studies were presented in an analytical framework in the initial panel meeting, and revisions and recommendations were formulated. In the present document, an extensive search of MEDLINE, National Library of Medicine's PubMed database, and Agency for Healthcare Research and Quality (AHRQ) Evidence Report and Technology Assessment was done using the keywords "*Chronic sinusitis*" or "*Chronic rhinosinusitis*", exploded to include *definition, classification, prevalence, epidemiology, diagnosis and therapy.*

The search was limited to articles involving adult (19 years old and above) humans, and those published in English from 2006 to 2015. The search yielded 718 articles, which included the following:

Meta-Analysis/ Systematic Reviews:	68
Randomized controlled trial (RCT):	91
Consensus report/CPG:	6

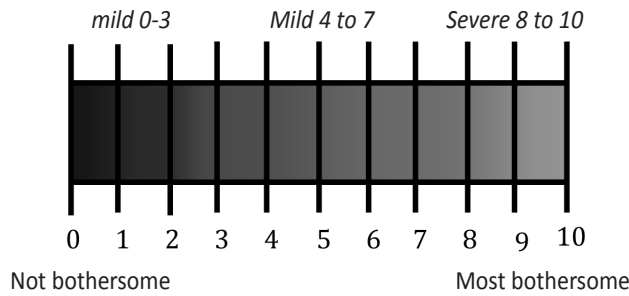
Additionally, older relevant literatures were included. A draft of the evidence-based recommendations (EBR) was collated and presented by the panel to the general assembly of ORL-HNS specialists.

primarily from the middle meatus; (b) nasal polyps; (c) edema/mucosal obstruction primarily in the middle meatus; (d) radiographic imaging showing mucosal changes within the ostiomeatal complex and/or sinuses.

*Grade A Recommendation, Level 1B Evidence*

The severity of the disease may be evaluated using a visual analog scale (Figure 1) in answer to the question of “how troublesome are your symptoms of rhinosinusitis”? This can help guide the clinician on the appropriate management.<sup>(3)</sup>

Figure 1: Visual Analog Scale (VAS)



**1.1. A distinction should be made if there is an acute exacerbation of CRS.**

*Grade B Recommendation, Level 2B Evidence*

Acute exacerbation of CRS is diagnosed when there is sudden deterioration of the patient’s condition with either worsening of baseline symptoms or development of additional symptoms. This is usually associated with bacterial infection.<sup>(1)</sup>

**1.2. CRS should be distinguished from Recurrent Acute Bacterial Rhinosinusitis**

*Grade B Recommendation, Level 2B Evidence*

Recurrent Acute Bacterial Rhinosinusitis (rABRS) is diagnosed when the patient has 4 or more episodes of Acute Bacterial Rhinosinusitis in a year *without* signs or symptoms of rhinosinusitis in between episodes.

<sup>(1)</sup> Though the symptom burden of CRS and rABRS is similar, distinction should be made between the two because antibiotic utilization is higher in rABRS.<sup>(4) (5) (6)</sup>

**2. The clinical diagnosis of CRS should be supported with objective documentation of sinonasal inflammation through anterior rhinoscopy and/or nasal endoscopy.**

*Grade A Recommendation, Level 1A Evidence*

Anterior rhinoscopy remains the first step in evaluating patients with this disease but it is of limited value. Nasal endoscopy (NE) is highly recommended for a thorough examination. It provides better illumination and visualization compared to anterior rhinoscopy. Likewise, it facilitates visualization of the sinus drainage pathways in the middle and superior meati as well as the nasopharynx.

In a systematic review by Wuister et al in 2014 comparing the diagnostic value of nasal endoscopy against CT scan as the gold-standard,

it was found that (+) NE findings afforded an added value of 25-28% for ruling-in CRS and (-) NE afforded an added value of 5-30% for ruling out CRS. The authors concluded that NE should be the first-line confirmatory test for diagnosing CRS.<sup>(7)</sup>

The Endoscopic Appearance Score<sup>(8)</sup> (Table 1) can be obtained at

**Table 1: Endoscopic Appearance Score<sup>(8)</sup>**

Characteristic	Baseline	3mos	6mos	1yr
Discharge, right (0,1,2)				
Discharge, left (0,1,2)				
Edema, right (0,1,2)				
Edema, left (0,1,2)				
Polyp, right (0,1,2,3)				
Polyp, left (0,1,2,3)				

\* Discharge: 0 – no discharge; 1 – clear, thin discharge; 2 – thick, purulent discharge

Edema: 0 – absent; 1 – mild; 2 – severe

Polyp: 0 – absence of polyps

1 – polyps in the middle meatus only

2 – polyps beyond the middle meatus but not blocking the nose completely

3 – polyps completely obstructing the nose

baseline and at regular intervals to monitor response to treatment.

**3. Multi-slice high resolution computed tomography scan may be used to confirm the diagnosis of CRS, especially in patients with a prolonged or complicated course, failed medical management and/or in whom surgery is contemplated. Plain sinus x-rays have a limited role in the diagnosis of CRS and is not recommended.**

*Grade B Recommendation, Level 2C Evidence*

Conventional computed tomography (CT) non-contrast scan demonstrates good sensitivity (85%) and above average specificity (59%) in diagnosing sinusitis in general.<sup>(9)</sup> The CT scan can aid in evaluating the extent of mucosal disease, patency of the sinus ostia and ostiomeatal complex, as well as the presence of anatomic abnormalities or tumors. It is recommended in failed medical therapy, in the presence of complications or in suspected malignancies. The anatomic detail the CT scan provides is also a useful roadmap for the surgeon during surgery. CT scan should be obtained in all patients who will undergo endoscopic sinus surgery.

High-resolution multi-slice CT (MSCT) shows advantage over conventional CT in demonstrating CRS. Superior image quality is obtained from coronal reconstructions from MSCT of the PNS compared with coronal reconstructions of single-slice CT (SSCT). There is absence of dental metal artifacts in coronal reconstructions of MSCT thus conferring superiority over direct coronal images of SSCT.<sup>(10)</sup> Images in all three planes (i.e. coronal, axial, sagittal) is recommended. In a study by Kew et al (2002), it was found that the addition of the parasagittal view improved the surgeon’s understanding of the anatomy of the frontal recess by a mean of 57% on a 10-point visual analogue scale. In fact, with the parasagittal scan, the surgical plan for the patient was altered in more than 50% of the patients studied.<sup>(11)</sup>

PNS x-rays are rapid, economical and non-invasive but give limited evaluation of the paranasal sinuses and the lower third of the nasal cavity. These have high specificity but 50% sensitivity in diagnosing CRS. The upright Waters view may suggest but cannot rule out the presence of sinusitis.<sup>(12)</sup>

**4. Maxillary aspirate or endoscopic-guided middle meatal swab culture and sensitivity may be done in cases of acute exacerbations of CRS.**

*Grade C Recommendation, Level 2A Evidence*

Maxillary aspirate culture and sensitivity is useful for establishing present local bacteriology and resistance, for patients who are immunocompromised, for those with severe infections, or for research purposes. Occasionally, endoscopic-guided middle meatal cultures may be done as an alternative to maxillary sinus puncture for obtaining cultures in patients with CRS<sup>(13)</sup>.

**5. Other tests may be done to further investigate modifying factors in the development of CRS as well as to assist in the evaluation of obstructive symptoms.**

*Grade C Recommendation, Level 3B Evidence*

Allergy skin testing and determination of serum IgE levels may be performed to diagnose allergic rhinitis and atopy. Although the relationship of allergy to CRS w/ and w/o NP remains controversial and results of studies are conflicting, determining the presence of this disease in the patient may still be helpful in choosing appropriate treatment options.<sup>(14)</sup>

Tests may be done to determine if the patient has bronchial asthma and/or sensitivity to aspirin. The presence of aspirin-exacerbated respiratory disease such as Samter's triad (i.e. aspirin sensitivity, asthma and nasal polyposis) has been shown to be associated with high recurrence rate of nasal polyps and 15-20% long-term revision surgery rate.<sup>(15)</sup>

Rhinomanometry and rhinometry can be useful in assessing airflow and nasal cavity volume. It can be useful for patients complaining of nasal obstruction to assess if it is a result of inflammation or a mechanical obstruction.<sup>(3)</sup>

**RECOMMENDATIONS ON THE TREATMENT OF CHRONIC RHINOSINUSITIS WITHOUT NASAL POLYPS (CRS w/o NP)**

**1. CRS w/o NP, being an inflammatory disease, should be primarily treated with intranasal corticosteroids (INCS)**

*Grade A Recommendation, Level 1A Evidence*

INCS improved symptom scores with minimal reported adverse effects in a Cochrane review of RCTs and 5 meta-analyses.<sup>(16)</sup>

A systematic review of RCTs done by Snidvongs (2013) on the efficacy of INCS concluded that there is enhanced effectiveness of INCS in patients with prior sinus surgery and with direct sinus delivery (i.e. steroid sinus irrigation)<sup>(17)</sup>

**2. Nasal saline irrigation (NSI) is recommended for management of CRS w/o NP.**

*Grade A Recommendation, Level 1A Evidence*

It has been reported in a Cochrane meta-analysis and several systematic reviews that NSI provide symptomatic relief in CRS.<sup>(18) (19) (20) (21)</sup> It has even been shown to be effective as sole treatment in CRS though its effect is not as significant as with the use of INCS.<sup>(18)</sup>

High-volume (>100ml) low-pressure saline irrigation is superior to saline spray in improving symptom scores. Similar symptom improvement is seen when comparing isotonic vs. hypertonic saline irrigations.<sup>(21) (22)</sup>

**3. CRS in acute exacerbation should be treated with short-term antibiotics.**

*Grade B Recommendation, Level 2B Evidence*

Short-term antibiotic treatment is defined as treatment duration shorter than 4 weeks. Amoxicillin-clavulanic acid, cefuroxime axetil and ciprofloxacin have been used with CRS in acute exacerbation with good clinical response.<sup>(3)</sup> INCS should be continued while the patient is on antibiotic therapy.

**4. Long-term, low dose macrolide therapy, lasting >12 weeks, is an option in the management of CRS w/o NP especially in those with normal or low total serum IgE levels**

*Grade B Recommendation, Level IIB Evidence*

Numerous open studies and one RCT have reported the efficacy of long-term, low dose macrolide as treatment for CRS with a response rate of 60-80%. Macrolides have been used for airway inflammatory disease due to its immunomodulatory activity rather than its antibacterial effect. Data suggests that CRS patients with normal or low total IgE (<250 U/ml) are more likely to respond to macrolide treatment compared to those with high serum IgE levels.<sup>(3)</sup> It has been shown to suppress neutrophilic inflammation in the airways.<sup>(23)</sup> Thus, macrolide treatment would most likely benefit patients with symptoms dominated by neutrophilic inflammation such as purulent discharge or postnasal drip.<sup>(2)</sup>

The recommended dosage regimen based on RCTs:

- a. Roxithromycin 150mg/day for 12 weeks<sup>(24)</sup>
- b. Clarithromycin 250mg/day for 12 weeks<sup>(25)</sup> or 500mg/day for 12 weeks<sup>(21)</sup>

Side-effects of long-term macrolide treatment should be considered such as development of antibiotic resistance, GI disorders, cardiac arrhythmia and hepatotoxicity.<sup>(2)</sup>

Long-term low-dose macrolide therapy may be given together with INCS especially when there is inadequate response to INCS alone.<sup>(21)</sup>

**5. Short-term oral steroids may be used in patients with severe disease, alone or in combination with other treatment options**

*Grade B Recommendation, Level IIB*

Oral steroids, in combination with antibiotics or INCS, have been shown to improve symptoms, radiologic findings and nasal endoscopy findings in patients with CRS w/o NP in several retrospective and prospective studies. However, there is lack of high quality RCTs to support the use of oral steroids, whether alone or in combination, for CRS w/o NP. <sup>(26)</sup>

**6. Mucolytics and decongestants have been traditionally used in the management of CRS, however there is no evidence supporting their use.**

*Grade C and D Recommendation, Level 4 and 5 Evidence respectively*

There were no RCTs found on the use of mucolytics and decongestants for the treatment of CRS w/o NP <sup>(3)</sup>

**7. Topical antibiotics, oral and topical antifungals and probiotics are not recommended in the management of CRS**

*Grade A(-) Recommendation, Level 1A Evidence*

Three RCTs using topical antibiotics for CRS showed no added benefit compared to saline. Likewise, no RCTs or systematic reviews for oral and topical antifungals and probiotics were found. These are not recommended for the management of CRS w/o NP. <sup>(3)</sup>

**8. Surgical management may be considered if the patient does not improve after 2-3 months of INCS treatment.**

*Grade A Recommendation, Level 1A Evidence*

Large prospective studies and case series have shown that endoscopic sinus surgery (ESS) is effective and safe for the management of patients with CRS w/o NP who have failed medical treatment. <sup>(3)</sup> Long-term success rates of ESS are high with over 90% symptomatic improvement. Greater improvement is seen in CRS w/ NP compared to CRS w/o NP. <sup>(1)</sup>

There is paucity of well-designed RCTs comparing medical vs. surgical treatment for CRS w/o NP. Based on a Cochrane review, the evidence shows that surgical management is just as effective as prolonged maximal medical management. Thus, ESS should be reserved for patients who have failed to improve with maximal medical treatment. <sup>(27)</sup> The reported incidence of complications from ESS ranges from 0.3 to 22.4%, majority of which are minor causing minimal patient morbidity. Major complications (i.e. CSF leak, orbital hemorrhage) occur in <1% of patients. <sup>(1)</sup>

**RECOMMENDATIONS ON THE TREATMENT OF CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS (CRS w/ NP)**

**1. The management of CRS w/ NP is primarily medical, with INCS as the first-line treatment option.**

*Grade A Recommendation, Level 1A Evidence*

INCS are indicated for long term treatment of CRS w/ NP. <sup>(28)</sup> Numerous systematic reviews support the efficacy of INCS in terms of symptom improvement, decrease in polyp size, prevention of polyp recurrence after surgery, improvement in nasal airflow and olfaction. <sup>(3) (29) (30)</sup>

Recommended INCS dosage regimens based on RCTs and local availability of the drug:

- Fluticasone propionate nasal spray 200mcg BID <sup>(31)</sup> or 400mcg/BID <sup>(32)</sup>
- Mometasone furoate nasal spray 200mcg OD <sup>(33)</sup> or 200mcg BID <sup>(34)</sup>

**2. Topical NSI is recommended for symptom relief in CRS w/ NP.**

*Grade A Recommendation, Level 1A Evidence*

Based on a Cochrane review, the benefits of topical NSI outweigh the minor side effects associated with its use. There is evidence that it has beneficial effects when used as a sole treatment modality but it is not as effective as INCS in CRS w/ and w/o NP. <sup>(18)</sup> The beneficial physiologic effects of NSI are improvement in ciliary beat activity and mucociliary clearance as well as removal of antigens, biofilms and inflammatory mediators. <sup>(2)</sup>

Studies have shown greater symptom improvement with high-volume saline irrigations. Recommended is a volume of 100-240 ml split between two nasal cavities once to three times per day. <sup>(21)</sup>

**3. Short-term oral steroids may be given as an adjunct treatment option for rapid though transient effects on polyp size reduction and symptom improvement.**

*Grade A Recommendation, Level 1A Evidence*

Systematic reviews have shown the short-term benefit of short courses of oral steroids (i.e. 2-4 weeks) with reduction in polyp size and subjective improvement in nasal symptom scores and quality of life. <sup>(35)</sup> Patient's response to a course of oral steroids may aid the clinician in deciding whether to continue with medical treatment or to consider surgery. Short-term treatment courses of systemic steroids combined with long term INCS led to satisfactory results in 85% of patients. If more than three systemic courses of oral steroids proved to be necessary for control of severe or progressive disease, a surgical option may be proposed. <sup>(36)</sup>

Suggested dosage regimen of steroids based on RCTs:

- a. Prednisolone 25mg/day for 2 weeks <sup>(37)</sup>
- b. Prednisone 30mg/day for 4 days then taper by 5mg every 2 days for a total of 2 weeks <sup>(38)</sup>
- c. Methylprednisolone 32mg/day for 5 days followed by 16mg/day for 5 days, then 8mg/day for 10 days <sup>(39)</sup>
- d. Methylprednisolone 16mg/day for 7 days <sup>(40)</sup>

Oral steroids may also be given perioperatively to improve surgical outcomes. In a double-blind RCT done by Wright et al (2007), patients treated with 30mg of prednisone 5 days preoperatively and 9 days postoperatively had technically less difficult surgery compared to placebo, as reported by the surgeon, and significantly healthier cavities postoperatively. <sup>(41)</sup>

**4. Long-term, low-dose macrolide treatment may be given as an option in CRS w/ NP, especially if there is poor response with INCS. Greater response is seen in patients with normal or low serum IgE or non-eosinophilic type of CRS w/ NP.**

*Grade B Recommendation, Level 2B Evidence*

There are few studies on the effect of long-term low-dose macrolide where the population was specifically defined into groups of CRS w/ or w/o NP. These studies showed a moderate effect on polyp size and patient symptoms.<sup>(3)</sup> Early studies by Suzuki et al (2000) showed that response to macrolide therapy was inversely related to serum IgE level and eosinophil counts in the sinus mucosa. He found no relation between response to macrolide therapy and tissue neutrophilia.<sup>(42)</sup> This was further corroborated by Haruna et al (2009) where he found poorer response to macrolides in CRS w/ NP. He found that there was statistically significant increase in the percentage of eosinophils in the sample polyp tissue of patients who had poor response to macrolide therapy.<sup>(43)</sup>

Some have proposed classifying CRS w/ NP into eosinophilic or non-eosinophilic due to difference in clinical profile and therapeutic response. Many regional studies suggest that there is increased prevalence of the non-eosinophilic type of nasal polyposis among Asians. Although at this time there is no single agreed-upon criterion for differentiating eosinophilic vs. non-eosinophilic polyps, a recommendation can be made to classify eosinophilic polyps in the presence of >5 eosinophils/hpf. This criterion was selected based on the preponderance of evidence correlating this cut-off to disease severity and clinical outcomes and due to its simplicity and practicality.<sup>(44) (45) (46) (47)</sup>

Due to lack of strong evidence supporting the use of long-term, low dose macrolide in CRS w/ NP and the possible side effects of this mode of treatment (i.e. antibiotic resistance, GI symptoms), the panel recommends reserving this for patients with poor response to INCS, low serum IgE and non-eosinophilic type of nasal polyps.

Suggested dosage regimen of macrolides based on uncontrolled trials<sup>(48)</sup>:

- a. Clarithromycin 400mg/day for at least 12 weeks
- b. Roxithromycin 150mg/day for at least 8 weeks

**5. Short-term treatment with Doxycycline may be given as a treatment option in CRS w/ NP**

*Grade A Recommendation, Level 1B Evidence*

One theory for the development of nasal polyps is the presence of Staphylococcus superantigens and targeting this mechanism is one way of treating CRS w/ NP. An RCT by Van Zele (2010) has shown that giving Doxycycline at 200mg on the first day followed by 100mg/tab once daily for a total of 20 days resulted in moderate though significant decrease in nasal polyp size, nasal symptoms and mucosal and systemic markers of inflammation.<sup>(39)</sup> The study population involved patients with recurrent nasal polyps after surgery for grade 3 polyps. Doxycycline may be given as an adjunct treatment which may benefit a subset of the population with CRS w/ NP.

**6. Leukotriene receptor antagonists (LTRAs) can be a treatment option especially in those with concomitant allergy.**

*Grade C Recommendation, Level IIB*

A recent systematic review (2015) showed that LTRAs, specifically Montelukast, may improve symptoms of CRS compared with placebo but there was no difference compared with INCS. Montelukast did not confer

additional benefit when used as an adjunct to INCS. Some studies have shown that LTRAs have greater effect in patients with concomitant allergic rhinitis, asthma and aspirin-exacerbated respiratory disease (AERD) but further studies are needed.<sup>(21) (49)</sup>

**7. Surgical management is recommended if there is failure of medical management.**

*Grade A Recommendation, Level 1A Evidence*

Failure of medical management implies that the patient still experiences CRS-specific symptoms that negatively affect quality of life and daily productivity. In mild to moderate persistent disease (i.e. VAS 0-7 and/or Grade 1-2 nasal polyps), ESS is an option if there is no improvement after 3 months of medical therapy. In severe persistent disease (i.e VAS 8-10 or grade 3 nasal polyp), ESS is an option if there is no improvement after 1 month of medical therapy.<sup>(3)</sup> Even with severe disease, giving initial medical treatment will have the added benefit of optimizing conditions for surgery. Surgical treatment temporarily relieves ostiomeatal complex blockage and serves primarily to facilitate the penetration of topical steroid therapy.<sup>(37)</sup>

Systematic review and large outcome studies have shown the safety and efficacy of ESS for CRS w/ NP. However, systematic reviews have shown no significant difference in benefits of medical vs. surgical management in terms of symptom scores and quality of life.<sup>(50)</sup> Thus, surgery is recommended if there is failure of medical management.

Several studies have shown that ESS is superior to other sinonasal procedures (i.e. polypectomy, Caldwell-Luc, radical nasalization and intranasal ethmoidectomy) with greater rates of complete relief of symptoms and better overall outcomes in terms of symptom score and disease recurrence. However, there are no studies comparing open sphenoethmoidectomy with ESS for CRS.<sup>(3) (51)</sup>

**8. Early postoperative care with use of nasal saline irrigation, debridement and corticosteroid (topical intranasal and/or oral) is strongly recommended. Other therapeutic interventions may be tailored to the patient's specific needs.**

*Grade B recommendation, Level 2A Evidence*

Postoperative use of INCS has been shown to significantly improve polyp score, patient's symptom scores and decrease the odds of polyp recurrence compared to placebo.<sup>(52)</sup>

**9. Measurement of subjective and objective treatment outcomes is recommended. Persistence or recurrence of disease will warrant further workups for modifying factors.**

*Grade D recommendation, Level 5 Evidence*

In a systematic review by Quintanilla-Dieck et al (2012), the most commonly utilized CRS-specific quality-of-life (QOL) instruments were the Sinonasal Outcomes Test (SNOT-22), the Rhinosinusitis Disability Index (RSDI) and the Chronic Sinusitis Survey (CSS).<sup>(53)</sup> Persistent or recurrent disease may indicate the possibility of previously unrecognized modifying factors such as immunodeficiency, AERD, allergy, odontogenic infection, laryngopharyngeal reflux, ciliary dysmotility, granulomatous disease and various other systemic diseases with sinonasal manifestations.<sup>(1)</sup>



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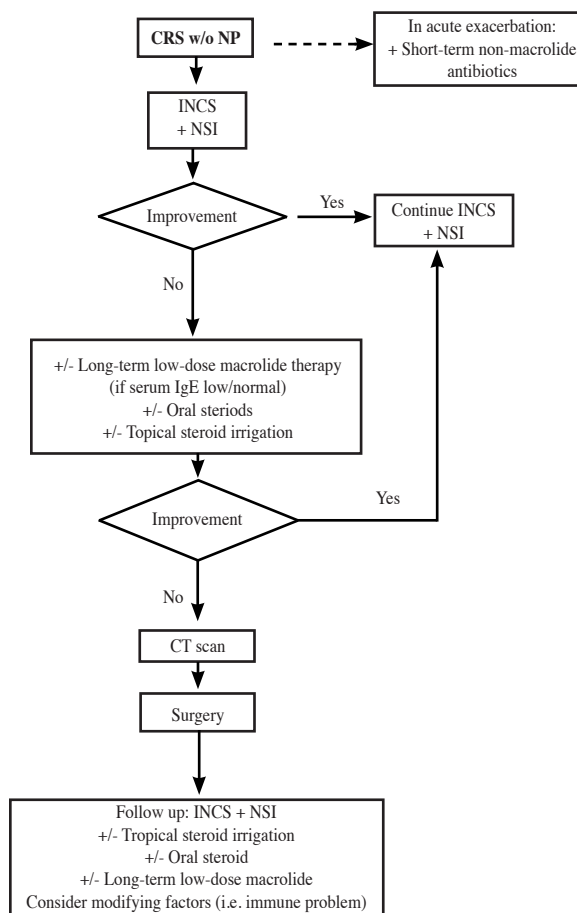
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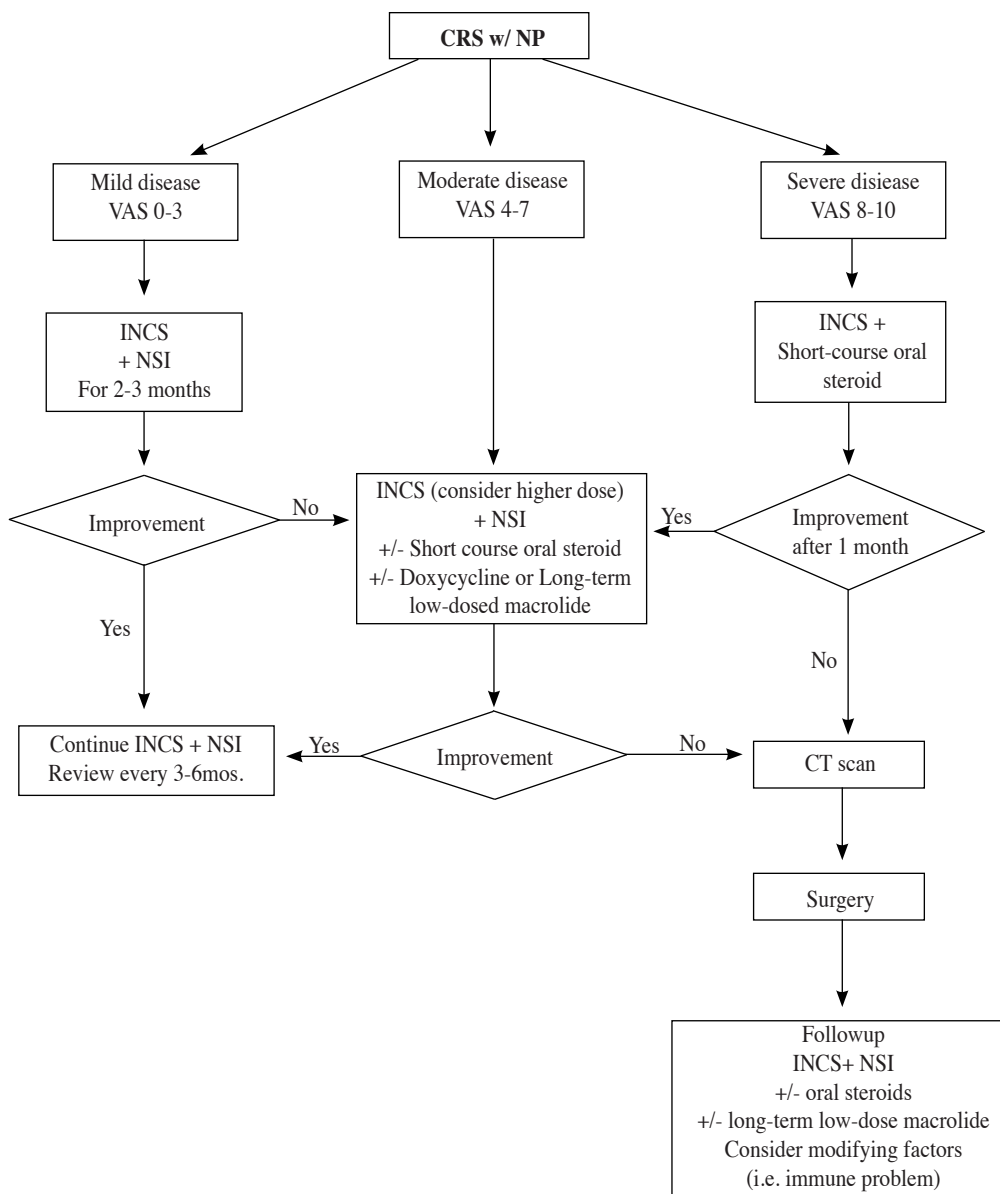
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