Low Dose Naltrexone & Autism Spectrum Disorder
In her 2006 report, Dr. Jaquelyn McCandless concluded, “As an effective, non-toxic, non-addicting, and inexpensive behavioral and immunomodulating intervention, LDN is joining our biomedical arsenal to help more and more children recover from autism as well as helping anyone with autoimmune diseases and cancer.”

Background - describe ASD and Epidemic Proportions

Diagnosis - new DSM 5.0 criteria

Treatment - Traditional therapies
  Medical therapies
  Biomedical therapies

LDN protocols

Recent Results

Conclusions
Autism Spectrum Disorders

An Alternative Biomedical Approach to Autism
Autism Spectrum Disorders

An Alternative Biomedical Approach to Autism
Autism Spectrum Disorders

An Alternative Biomedical Approach to Autism
Autism Spectrum Disorders

- Phenotypic presentation
- Toxic environment
- Individual susceptibility
- Phenotypic presentation

? Cause(s)
Autism Spectrum Disorder

- Learning
  - Cognition
  - Reading
  - Arithmetic

- Repetitive movement
- Communication
  - Apraxia
  - Delay
  - Articulation
  - Verbal stims
  - Echolalia
  - Scripting

- Social isolation
- Sensory issues
  - Visual
  - Auditory
  - Tactile
  - Taste
  - Smell

- Restricted interests

- Behavioral issues
  - ADHD
  - Learning
  - Focus
  - Anxiety
  - Tantrums
  - Oppositional
  - Immaturity

- Immune regulation
  - Allergies
  - Eczema
  - Asthma
  - Otitis media

- G-I Problems
- Hypotonia

- Sleep disturbances

- Eye contact
- Seizures
Autism Spectrum Disorder
Implementation of DSM 5.0
Autism Spectrum Disorder

DSM IV to DSM 5.0:

- Speech and Language
- Social
- Movement

Early and Significant
Autism Spectrum Disorder

DSM-5 Autism Spectrum Disorder

Persistent social communication & social interaction
- Deficits in social-emotional reciprocity
- Deficits in nonverbal communicative behaviors used for social interaction
- Deficits in developing, maintaining and understanding relationships

? SEVERITY

Restricted & repetitive behavior patterns
- Stereotyped or repetitive motor movements
- Insistence on sameness or inflexible adherence to routines highly restricted, fixated interests
  OR
- Hyper or hyper reactivity to sensory input
  Unusual interest in sensory aspects of the environment

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Autism Spectrum Disorders

Types

Genetic – Fragile X, Rett’s S., Trisomy 21?, Copy number variations

Gastro-intestinal
   Most common in practice
   If a person acts like they have ‘ants in their pants’, sometimes they actually do!

Immunologic – Asthma, eczema, food sensitivities, frequent ear infections, ?vaccination
   Microbiome alterations

Syndromes – Down’s S., Metabolic disturbances, Unclassified

Birth complications – Cerebral palsy, ‘Mental Retardation’, “Premies”

Metabolic & Nutritional – Vitamin deficiency, Lipid abnormalities, Picky eaters, MTHFR

Boy vs. Girl

Early vs. Late
Autism Spectrum Disorders
Medical Workup

H&P

Specialized
  Audiology
  MRI
  EEG

Chromosomes

CBC

Metal Levels

Thyroid Screen

Appropriate additional baseline information
Autism Spectrum Disorders
Medical Workup

G-I Health –
Comprehensive evaluation
*Toilet training can be much more effective when gut health is restored.*

Food Allergies –
The presence of immunoglobulins indicates inflammation results.
Reducing overall energy-depleting reactions for use elsewhere

Vitamin levels –
Low levels in most of our patients
D3 especially important in immune health

Comprehensive metabolic profile
Baseline, drug tolerance and interactions

Lipid panel
High – nutrition?
Low – eye contact, immune health
Autism Spectrum Disorders
Available Treatments

Conventional
Anxiety
- Abilify
- Risperdal
- Intuniv

Stimulant
- Methamphetamine
- Ritalin
- Strattera

SSRI
- Zoloft
- Prozac

Anti-Seizure
- Trileptal
- Depakote
Autism Spectrum Disorders
Available Treatments

Alternative
- Homeopathic
- Naturopathic
- Chelation
- Cranial-sacral
- NAET
- MMS
- Helminth
- HBOT
- Stem cell therapies

Biomedical
- Gut health
- Nutritional optimization
- Immune regulation

Traditional
- OT, PT, S&L
- ABA
Autism Spectrum Disorders

Treatment – depends on underlying conditions(s), age and severity of:

Behavioral difficulties –
   Especially aggression, self-injurious, destructive

Speech apraxia –
   No conventional treatment exists
Autism Spectrum Disorders & Low Dose Naltrexone

B-endorphin disregulation in autistic and self-injurious behavior: A neurodevelopmental hypothesis

Curt A. Sandman Ph.D.*

Article first published online: 12 OCT 2004
DOI: 10.1002/syn.890020304

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Autism Spectrum Disorders & Low Dose Naltrexone

B-endorphin disregulation in autistic and self-injurious behavior: A neurodevelopmental hypothesis. Curt A. Sandman Ph.D.*, et. al. 1988

Certain peptides influence neurodevelopmental processes.

Earlier studies indicated that some of those compounds improved behavioral efficiency in retarded individuals.

Recent studies have shown that opiate blockers reduce treatment-resistant self-injurious behaviors.

Prenatal protein dysregulation, addiction to endogenous opiates and elevated pain threshold have been proposed to account for this behavior.
Autism Spectrum Disorders & Low Dose Naltrexone

B-endorphin disregulation in autistic and self-injurious behavior: A neurodevelopmental hypothesis. Curt A. Sandman Ph.D.*, et. al. 1988

In study one, four SIB patients were given 0, 25, 50 or 100 mg of naltrexone on separate weeks in a double blind, Latin square design. A specific dose dependent reduction in SIB was observed in three patients.

In study two, plasma b-endorphin was measured in 40 patients with SIB, a related behavior, stereotypy (ST) or controls. SIB and ST patients had higher levels of endorphin than controls.

These data added new support for the role of b-endorphin in a treatment-resistant patient group.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone in Autistic Children: An Acute Open Dose Range Tolerance Trial

MAGDA CAMPBELL, M.D., JOHN E. OVERALL, Ph.D., ARTHUR M. SMALL, M.D., MAE S. SOKOL, M.D., ELIZABETH KAY SPENCER, M.D., PHILLIP ADAMS, Ph.D., RODGER L. FOLTZ, Ph.D., KIM M. MONTI, B.S., RICHARD PERRY, M.D., MITCHELL NOBLER, M.D., EUGENE ROBERTS, Ph.D.
Autism Spectrum Disorders & Low Dose Naltrexone


The safety and efficacy of naltrexone was explored in an open acute dose range tolerance trial in 10 hospitalized autistic children, ages 3.42 to 6.50 years (mean, 5.04).

Naltrexone was given in ascending doses: 0.5, 1.0, and 2.0 mg/kg/day.

Behavioral side effects were observed as early as ½ hour after dosing.

Ratings on the Children's Psychiatric Rating Scale showed that withdrawal was reduced across all three dose levels

0.5 mg/kg/day dose resulted in increased verbal production

2.0 mg/kg/day dose resulted in reduction of stereotypies.
Mild sedation of brief duration was the only side effect.

Electrocardiogram, liver function tests, and all other laboratory studies remained unchanged throughout the study.

These preliminary findings require replication in a larger sample of patients under double-blind and placebo controlled condition.
Autism Spectrum Disorders & Low Dose Naltrexone


18 autistic children, aged 3.08–7.99 yrs. Randomly assigned to NAL or placebo and received daily doses over a period of 21 days. NAL was superior to placebo according to blind clinical global consensus ratings.

Other behavioral rating measures, such as the Children's Psychiatric Rating Scale (W. Guy, 1976) did not confirm this result.

There was only a suggestion that NAL reduced fidgety and hyperactive behavior and tended to alleviate overall symptomatology in older children.

NAL did not appear to affect discrimination learning.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone and other potential new pharmacological treatments of autism.
Panksepp, Jaak; Lensing, Patrick; Leboyer, Marion; Bouvard, Manuel P.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone and other potential new pharmacological treatments of autism. Panksepp, Jaak; Lensing, Patrick; Leboyer, Marion; Bouvard, Manuel P.

Summarizes results from a series of open and double-blind trials that have yielded positive therapeutic effects with low doses of naltrexone, including: reductions in autistic stereotypes, aggressiveness, and self-injurious behaviors, and the production of heightened prosocial emotional attitudes that are accompanied by increased smiling, eye contact, attention, and attempts to communicate.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone and other potential new pharmacological treatments of autism.
Panksepp, Jaak; Lensing, Patrick; Leboyer, Marion; Bouvard, Manuel P.

The positive behavioral change seems to be enhanced by social support, and how such features of therapeutic situations can be maximized to optimize clinical benefits… is discussed.
Autism Spectrum Disorders & Low Dose Naltrexone

Case Study

Naltrexone in Autistic Children: Behavioral Symptoms and Attentional Learning

MAGDA CAMPBELL, M.D., LOWELL T. ANDERSON, PH.D., ARTHUR M. SMALL, M.D., PHILLIP ADAMS, PH.D., NILDA M. GONZALEZ, M.D., MONTIQUE ERNST, M.D., PH.D.
Autism Spectrum Disorders & Low Dose Naltrexone

Magda Campbell MD, et. al. 1993

Objective
To assess critically the short-term efficacy and safety of naltrexone in autistic children and its effects on discrimination learning in the laboratory.

Method
Forty-one children, all inpatients, ages 2.9 to 7.8 years, completed the study. Naltrexone reduced hyperactivity and had no effect on discrimination learning in the laboratory. There was a suggestion that it had a beneficial effect on decreasing self-injurious behavior.

Untoward effects were mild and transient.
Conclusion
In the present study, naltrexone significantly reduced only hyperactivity, and no serious untoward effects were observed.

The effectiveness of naltrexone in the treatment of autism and self-injurious behavior requires additional assessment in a sample of children with moderate to severe self-injurious behavior.
Autism Spectrum Disorders & Low Dose Naltrexone

Journal of the American Academy of Child & Adolescent Psychiatry

Volume 34, Issue 2, February 1995, Pages 223–231

ARTICLE

Naltrexone in Young Autistic Children: A Double-Blind, Placebo-Controlled Crossover Study

Barbara K. Kolmen, M.D. 🌀, Heidi M. Feldman, M.D. Ph.D., Benjamin L. Handen, Ph.D., Janine E. Janosky, Ph.D.

From the Child Development Unit, Children's Hospital of Pittsburgh, Departments of Pediatrics (Drs. Kolmen, Feldman, and Handen), Psychiatry (Dr. Handen), and Clinical Epidemiology (Dr. Janosky), University of Pittsburgh School of Medicine.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone in Young Autistic Children: A Double-Blind, Placebo-Controlled Crossover Study Barbara K. Kolmen, M.D., et. al. 1995

Objective
This study evaluated the efficacy and safety of naltrexone an opiate blocker, in the treatment of autism.

Method
Thirteen children with autistic disorder, aged 3.4 to 8.3 years (mean 5.4)

Naltrexone, 1.0 mg/kg, was given daily in a randomized, double-blind, placebo-controlled crossover design.

Dependent measures included parent and teacher Clinical Global Impressions (CGI), Conners Rating Scales, and Naltrexone Side-Effects (SE) Rating Scale; laboratory CGI, movement actometer readings, and a 10-second interval recording system analysis of on-task, communication initiations, disruptive behavior, and self-stimulation.
Results
Eight of 13 subjects improved in two or more settings. Changes in parent measures... and Teacher CGI achieved statistical significance. Teacher SE-Restlessness and initiation of communication in the clinic showed a trend toward improvement. Actometer readings improved in two children who were very active at baseline. Adverse side effects were behavioral, mild, and transient. Administering the bitter tablet was a challenge.

Conclusion
Naltrexone offers promise as an agent for modest improvement of behavior and social communication in young children with autism. Parent and teacher measures can be useful in outpatient trials to evaluate change.
Low-dose naltrexone effects on plasma chemistries and clinical symptoms in autism: a double-blind, placebo-controlled study

Manuel P. Bouvard\textsuperscript{a}, Marion Leboyer\textsuperscript{b}, Jean-Marie Launay\textsuperscript{c}, Christophe Recasens\textsuperscript{a}, Marie-Hélène Plumet\textsuperscript{a}, Delphine Waller-Perotte\textsuperscript{a}, François Tabuteau\textsuperscript{c}, Dominique Bondoux\textsuperscript{c}, Michel Dugas\textsuperscript{a}, Patrick Lensing\textsuperscript{d}, Jaak Panksepp \textsuperscript{e}.
Abstract
Month-long naltrexone (NTX) treatment at a daily oral dose of 0.5 mg/kg/day vs. Placebo
Modest clinical benefits were achieved with both… marginally better overall results NTX.
Degree of improvement appeared to be related to plasma chemical profiles.
Massively elevated levels of β-endorphin were observed in all children.
70% of the children exhibited abnormally low levels of adrenocorticotropic hormone, elevated norepinephrine (60%) arginine-vasopressin (50%) and serotonin (20%).
Autism Spectrum Disorders & Low Dose Naltrexone


The best clinical responders exhibited the clearest normalization of the elevated plasma chemistries, especially in C-terminal-β-endorphin and serotonin.

The results suggest that NTX only benefits a subgroup of autistic children, who may be identified by the presence of certain plasma abnormalities.
Autism Spectrum Disorders & Low Dose Naltrexone

Placebo-controlled acute dosage naltrexone study in young autistic children

Sophie H.N. Willemsen-Swinkels, Jan K. Buitelaar, Florence G. Weijnen, Herman van Engeland
Placebo-controlled acute dosage naltrexone study in young autistic children
Sophie H.N., et. al. 1995

Double-blind, placebo-controlled, crossover trial
23 autistic children were treated with a single 40-mg dose naltrexone
Naltrexone treatment failed to produce significant changes in social behavior,
reduced irritability and target scores on behavior checklists.

The playroom data indicated that naltrexone significantly affected indices of
activity and attention.
Autism Spectrum Disorders & Low Dose Naltrexone

Opioid-immune interactions in autism: behavioural and immunological assessment during a double-blind treatment with naltrexone

Renato SCIFO (a), Matteo CIONI (b), Alfredo NICOLOSI (c), Nunzio BATTICANE (b), Cataldo TIROLO (b), Nuccio TESTA (b), Maria C. QUATTROPANI (d), Maria C. MORALE (b), Francesco GALLO (e) and Bianca MARCHETTI (e)
Autism Spectrum Disorders & Low Dose Naltrexone

Opioid-immune interactions in autism: behavioural and immunological assessment during a double-blind treatment with naltrexone. Scifo R1, et. al. 1996

12 patients, 7 to 15 years

Double-blind crossover study with NAL at the doses of 0.5, 1.0 and 1.5 mg/kg q48 hours.

Responders – 7/12 displayed “… a significant reduction of the autistic symptomatology.”

The behavioural improvement was accompanied by alterations in the distribution of the major lymphocyte subsets, with a significant increase of the T-helper-inducers (CD4+CD8-) and a significant reduction of the T-cytotoxic-suppressor (CD4-CD8+) resulting in a normalization of the CD4/CD8 ratio.

Changes in natural killer cells and activity were inversely related to plasma beta-endorphin levels.
Opioid-immune interactions in autism: behavioural and immunological assessment during a double-blind treatment with naltrexone. Scifo R1, et. al. 1996

It is suggested that the mechanisms underlying opioid-immune interactions are altered in this population of autistic children and that an immunological screening may have prognostic value for the pharmacological therapy with opiate antagonists.
Autism Spectrum Disorders & Low Dose Naltrexone

Biological Psychiatry
Volume 39, Issue 12, 15 June 1996, Pages 1023–1031

The effects of chronic naltrexone treatment in young autistic children: A double-blind placebo-controlled crossover study
Sophie H.N. Willemsen-Swinkels, Jan K. Buitelaar, Herman van Engeland
Autism Spectrum Disorders & Low Dose Naltrexone


23 autistic children, aged 3–7 years
Mean daily dosage of 1 mg/kg naltrexone for 4 weeks.

On average, parents' checklists and playroom data could not differentiate between naltrexone treatment and placebo treatment; however, teachers significantly favored naltrexone treatment.

They reported a decrease in hyperactivity and irritability. No effects of naltrexone on social and stereotypic behavior could be demonstrated.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone in Young Autistic Children: Replication Study and Learning Measures

Barbara K. Kolmen, M.D. 🌟, Heidi M. Feldman, M.D., Ph.D., Benjamin L. Handen, Ph.D., Janine E. Janosky, Ph.D.
Autism Spectrum Disorders & Low Dose Naltrexone

Naltrexone in Young Autistic Children: Replication Study and Learning Measures

This study expanded upon previous work on naltrexone efficacy and safety in young autistic children and assessed performance on learning measures.

Method
Eleven children with autistic disorder, aged 3.0 to 8.3 years
Naltrexone, 1.0 mg/kg, was given daily in a randomized, double-blind, crossover design.

Results
…The combined study sample showed improvement on all parent measures and on Teacher CGI and SE-Restlessness compared with baseline and placebo.
Eleven of the 24 children improved in two or more settings.
Scores on learning measures did not change across conditions.

Conclusions
Naltrexone was associated with modest improvement of behavior in 11 of 24 children, but learning did not improve.
Autism Spectrum Disorders & Low Dose Naltrexone

Journal of the American Academy of Child & Adolescent Psychiatry
Volume 38, Issue 5, May 1999, Pages 587–593

Special Section

Naltrexone and Communication Skills in Young Children With Autism

HEIDI M. FELDMAN, M.D., PH.D., BARBARA K. KOLMEN, M.D., ALDA MARIA GONZAGA, B.A.
**Autism Spectrum Disorders & Low Dose Naltrexone**


**Objectives**
To evaluate the effect of naltrexone on communication skills of young children with autism.

**Method**
Twenty-four children with autism, 3.0 to 8.3 years old (mean 5.1) - randomized, double-blind, placebo-controlled, crossover trial. Naltrexone, 1.0 mg/kg, or placebo was administered daily for 2 weeks. Communication was evaluated from videotaped samples of seminaturalistic parent-child interaction.
Autism Spectrum Disorders & Low Dose Naltrexone

The effects of chronic naltrexone treatment in young autistic children: A double-blind Naltrexone and Communication Skills in Young Children With Autism
H.M. Feldman, M.D., et. al. 1999

Results
No differences were found between the naltrexone and placebo conditions in any of the measures of children or parents' communication.

Significant correlations were found between the child's number of words and developmental quotient (Spearman $p = 0.58$, $p = .003$) and between the child's and parent's number of words ($p = 0.55$, $p = .005$).

Conclusions
In this short-term study, the medication did not lead to improvement in communication, a core deficit of autism.
Autism Spectrum Disorders & Low Dose Naltrexone

Self-injurious behavior and the efficacy of naltrexone treatment: A quantitative synthesis

Frank J. Symons†, Andrea Thompson and Michael C. Rodriguez

Article first published online: 20 DEC 2004
DOI: 10.1002/mrdd.20031

Mental Retardation and Developmental Disabilities Research Reviews

Special Issue: Treatment Efficacy

People with mental retardation, autism, and related developmental disabilities who self-injure are treated with a wide array of behavioral techniques and psychotropic medications.

Despite numerous reports documenting short-term and some long-term changes in self-injury associated with the opiate antagonist naltrexone hydrochloride, no quantitative review of its efficacy has been reported.

A quantitative synthesis of the peer-reviewed published literature from 1983 to 2003 documenting the use of naltrexone for the treatment of self-injurious behavior (SIB). Individual-level results were analyzed given subject and study characteristics.
Self-injurious behavior and the efficacy of naltrexone treatment: A quantitative synthesis. Frank J. Symons†*, et. al. 2004

A sample of 27 research articles involving 86 subjects with self-injury was reviewed.

Eighty percent of subjects were reported to improve relative to baseline (i.e., SIB reduced) during naltrexone administration and 47% of subjects SIB was reduced by 50% or greater.

Males were more likely than females to respond.

No significant relations were found between treatment outcomes and autism status or form of self-injury.

Results are discussed with respect to future efficacy work related to study outcomes and the pharmacological treatment of self-injury.

OBJECTIVE: To review the efficacy and safety of naltrexone in pediatric patients with autistic disorder (AD).

DATA SOURCES: Literature search
Three case reports, 8 case series, and 14 clinical studies were identified as pertinent.

DATA:
Naltrexone has been used most commonly at doses ranging from 0.5 to 2 mg/kg/day Found to be predominantly effective in decreasing self-injurious behavior.

DATA:
Naltrexone may also attenuate hyperactivity, agitation, irritability, temper tantrums, social withdrawal, and stereotyped behaviors. Patients may also exhibit improved attention and eye contact. Transient sedation was the most commonly reported adverse event.

CONCLUSIONS:
A child affected by AD may benefit from a trial of naltrexone therapy, particularly if the child exhibits self-injurious behavior and other attempted therapies have failed. Serious adverse effects have not been reported in short-term studies.
I completed a preliminary eight-week informal study on 15 of my autism patients May-June 2005 applying 3mg of LDN transdermally between 9 and 12 p.m.

Eight of the 15 children in this study had positive responses, with five of these eight having results considered quite phenomenal according to their parents.

The primary positive responses are in the area of mood regulation, cognition, language, and socialization.

Two small children responded better when changed to 1-1/2mg dosing.
No allergic reactions were noted, and the primary negative side effect was insomnia and earlier awakening, usually fairly short-lived.

As an effective, non-toxic, non-addicting, and inexpensive behavioral and immunomodulating intervention, LDN is joining our biomedical arsenal to help more and more children recover from autism as well as helping anyone with autoimmune diseases and cancer.

As an FDA approved medication, it must be prescribed and must also be compounded for the tiny dosing required.
During 2014, 53 patients chosen out of 393 total visits
Received 3mg/1cc as cream after 9PM

<table>
<thead>
<tr>
<th>Response to LDN Treatment</th>
<th>Number of Patients (out of 53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Significant Improvement”</td>
<td>5</td>
</tr>
<tr>
<td>“Satisfactory Results”</td>
<td>19</td>
</tr>
<tr>
<td>“No Improvement/Unsatisfactory Results”</td>
<td>16</td>
</tr>
<tr>
<td>“No Follow-Up Information Received”</td>
<td>4</td>
</tr>
<tr>
<td>“LDN Prescribed but Usage Not Initiated”</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 10.1 Responses to LDN Treatment by ASD Patients.
Autism Spectrum Disorders & Low Dose Naltrexone

Jacob’s Story
Autism Spectrum Disorders & Low Dose Naltrexone

Success depends on:

Accurate diagnosis

Choose candidates most likely to succeed

Address gut and metabolic issues first

Address other co-morbidities as they exist or arise
Autism Spectrum Disorders & Low Dose Naltrexone

Form
Liquid?
  Pill?
  Cream?

Expectations
  First few days
  Few weeks
  Long term

Side effects
  5% stop
  25% Renew
  70% Not enough/ no effect
Autism Treatment in the First Year of Life: A Pilot Study of Infant Start, a Parent-Implemented Intervention for Symptomatic Infants

S. J. Rogers, L. Vismara, A. L. Wagner, C. McCormick, G. Young, S. Ozonoff
Treatment Works

12-week, low-intensity treatment with seven symptomatic infants ages 7–15 months

Parents mastered the intervention and maintained skills after treatment ended

Four comparison groups were matched from a study of infant siblings

The treated group of infants was significantly more symptomatic than most of the comparison groups at 9 months of age but was significantly less symptomatic than the two most affected groups between 18 and 36 months.

At 36 months, the treated group had much lower rates of both ASD and DQs under 70 than a similarly symptomatic group who did not enroll in the treatment study.
Conclusions

LDN – Autism - 2016
Autism Spectrum Disorder

Complex, multi-system condition leading to behavioral and developmental signs and symptoms.

Epidemic proportions

Treatable condition – combination of therapies and medical intervention at earliest stages provides best chance for recovery
Continuum of brain, gut, inflammation protocols

Anecdotal evidence - Small sample size, and inconsistent evaluative methods

Few therapeutic breakthroughs
  Learning more about genetics and susceptibility
  Learning more about environmental effects

Given risks, in highest responder population, Naltrexone worth a try

Continuing problems
  Education
  Older patients