

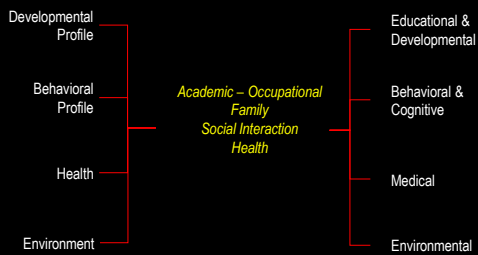
## The ABCs of ADHD

Eric Tridas, MD  
 Courage to Risk Conference  
 Colorado Springs, CO  
 January 2010

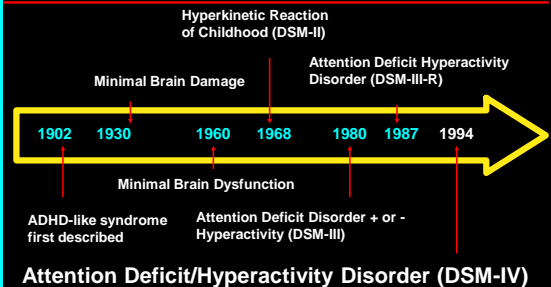
## Disclosures

- Dr. Tridas is a speaker for:
  - Eli Lilly
  - McNeil
  - Novartis
  - Shire
- Dr. Tridas is a consultant for:
  - Eli Lilly
  - McNeil
  - Novartis
- Dr. Tridas does research for:
  - Eli Lilly

## The Developmental Web



## ADHD: Historical Timeline



## Diagnostic Criteria for ADHD: DSM-IV

- Persistent symptoms of inattention and/or impulsivity and hyperactivity
- Onset of symptoms before age 7
- Impairment in 2 or more settings (eg, school, work, home)
- Evidence of clinically significant impairment in social, academic, or occupational functioning
- Symptoms not a result of other disorders

Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Text Revision.  
 Washington, DC: American Psychiatric Association; 2000.

## DSM-IV Diagnostic Criteria Symptoms for ADHD

- Inattention ( $\geq 6$ )
  - Is careless
  - Has difficulty sustaining attention in activity
  - Does not listen
  - Does not follow through with tasks
  - Is disorganized
  - Avoids/dislikes tasks requiring sustained mental effort
  - Loses important items
  - Is easily distracted
  - Is forgetful in daily activities

Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Text Revision.  
 Washington, DC: American Psychiatric Association; 2000.

# DSM-IV Diagnostic Criteria Symptoms for ADHD (cont'd)

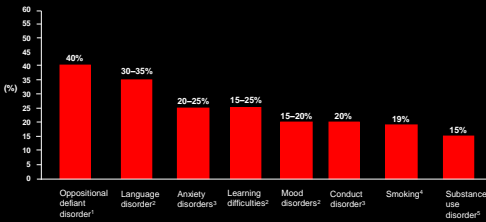
- Hyperactivity (≥6)
  - Squirms and fidgets
  - Cannot stay seated
  - Runs/climbs excessively
  - Cannot play/work quietly
  - Is on the go/driven by a motor
  - Talks excessively
- Impulsivity
  - Blurts out answers
  - Cannot wait turn
  - Intrudes/interrupts others

Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Text Revision. Washington, DC: American Psychiatric Association; 2000.

# ADHD: DSM-IV Subtypes

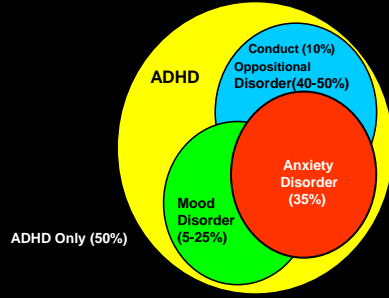
- ADHD **Combined Type**
  - Criteria are met for both inattention and impulsivity/hyperactivity (≥ 6 of each)
- ADHD **Inattentive Type**
  - Criteria met for inattention but not for impulsivity/hyperactivity (≥ 6)
- ADHD **Hyperactive-Impulsive Type**
  - Criteria met for impulsivity/hyperactivity but not for inattention (≥ 6)

# ADHD: Comorbid Conditions



MTA Cooperative Group. Arch Gen Psychiatry 1999; 56:1076-1086.  
Barkley R. Attention-deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, 2nd ed. New York: Guilford Press, 1993.  
Rowdenman J, et al. Am J Psychiatry 1991; 148:505-517.  
Millberger S, et al. J Am Acad Child Adolesc Psychiatry 1997; 36:37-44.  
Rowdenman J, et al. J Am Acad Child Adolesc Psychiatry 1997; 36:21-28.

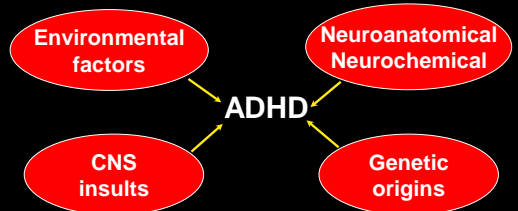
# Comorbidities Common With ADHD



# Etiology

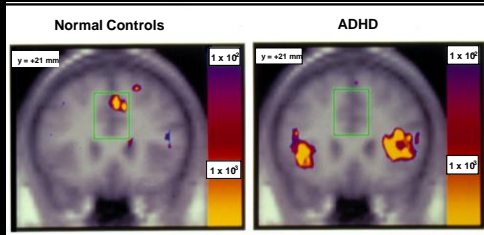
# Etiology

ADHD is a heterogeneous behavioral disorder with multiple possible etiologies



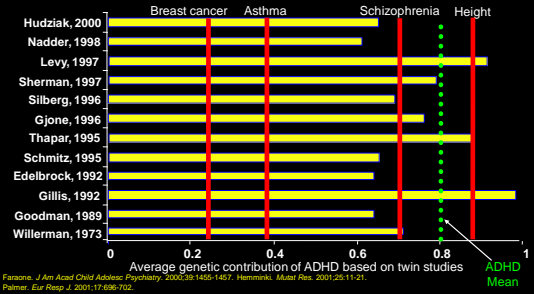
CNS = central nervous system.

## A Variety of Functional & Structural Differences Appear in the ADHD Brain



MGH-NMR Center & Harvard-MIT CTFP. Reprinted by permission of Elsevier. Science from Anterior cingulate cortex dysfunction in ADHD revealed by fMRI and the Counting Stroop, by Bush G, Frazier JA, Rauch SL, et al. *Biological Psychiatry* 45(12), Copyright 1999 by the Society of Biological Psychiatry.

## Twin Studies Show ADHD Is a Genetic Disorder



Faraone, *J Am Acad Child Adolesc Psychiatry* 2000;39:1459-1467, Henkens, *Mult Res*, 2001;25:1121, Plomin, *Eur Hosp J* 2001;17:690-702.

## Impairment Caused by ADHD

*How does it present?  
Impact on quality of life*

## Impairment

Academic  
Family  
Socialization  
Medical

## Impairment

- ADHD is a disorder of performance, not skill
- ADHD disrupts executive function
- ADHD creates problems with self-regulation
- ADHD increases health risks

## Impairment

- ACADEMIC  
– *Production vs. Knowledge*
- FAMILY  
– *Spacey/Over-Reactive vs. Defiant*
- SOCIALIZATION  
– *Insatiable vs. Malicious*
- MEDICAL  
– *Cigarette smoking, Car accidents, SUD*

## ADHD: Impairment



## ADHD: Impact on Family

Parents of children with ADHD experience higher levels of:



- Stress
- Self-blame
- Social isolation
- Depression
- Marital discord

Mash and Johnston, J Clin Child Psychol, 1990;19:313.  
Murphy and Barkley, Am J Orthopsychiatry, 1996;66:93.

## ADHD : Adults Performance Limitations

- Despite similar educational levels and IQ scores, non-medicated adults with ADHD display:
  - Significantly more academic difficulty in school (25% repeat a grade)
  - Lower levels of occupational advancement

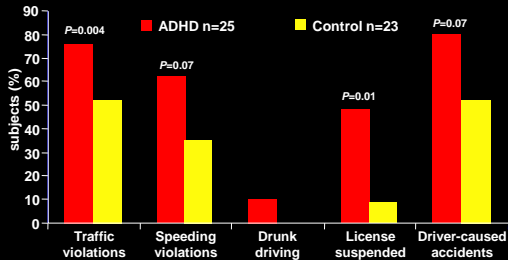
Faraone S, et al. Biol Psychiatry, 2000;48:9-20.  
Biederman, et al. Am J Psychiatry, 1993;150:1792-1798.

## ADHD Affects Socialization

- Children are stigmatized by their behavior
  - Disruptive behavior
    - Troublemakers
    - Bad sportsmanship
    - Excessive talking
    - Cannot sit still
    - Unfocused, not responsive to others
    - Impulsive aggression
  - Immaturity and impulsiveness
    - Center of attention
    - Breaks the rules
    - Blurting out answers
    - Peer rejection
- Adolescents continue to demonstrate social problems
  - Poor participation in group activities
  - Few friends
  - Vulnerable to antisocial groups, drug abuse

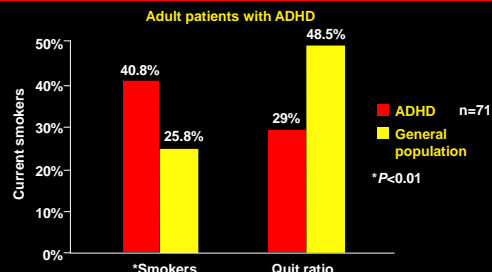
MCAP, J Am Acad Child Adolesc Psychiatry, 1997;36:855-1215.  
Barkley RA, J Am Acad Child Adolesc Psychiatry, 1991;30:152-161.

## Increased Traffic Violations and Motor Vehicle Accidents in Adolescents and Adults with ADHD



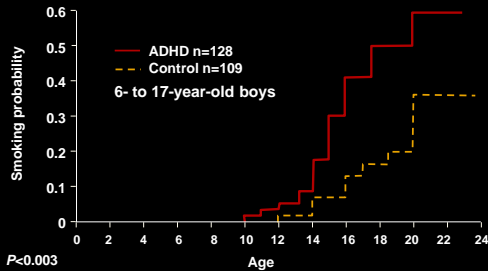
Barkley RA, et al. Pediatrics, 1996;98:1089-1095.

## Increased Smoking with ADHD



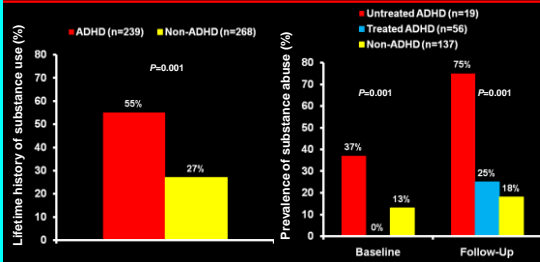
Pomerleau, et al. J Subst Abuse, 1995;7:373-378.

## Earlier Initiation of Smoking with ADHD



Mbergert S, et al. *J Am Acad Child Adolesc Psychol*. 1997;36:37-44.

## Untreated ADHD Is Associated With Higher Risk of Substance Abuse



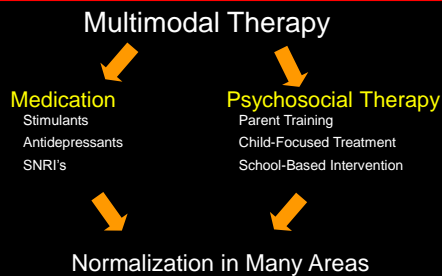
Biederman J, et al. *Biol Psychiatry*. 1998;44:269-273.  
Biederman J, et al. *Pediatrics*. 1999;104:e20-e25.

## Adolescent & Adult Outcome

- Symptoms Persist in 50-65%
- Associated Problems
  - Conduct
  - Emotional
  - Socialization
  - Education
  - Employment
- Satisfactory Outcome in 60-70%

## Management of ADHD

## Good Management of ADHD Involves Multimodal Therapy



## MTA Study Objective and Design

### Objective:

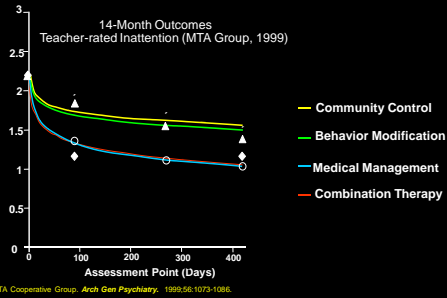
- To compare the long-term efficacy of pharmacotherapy, behavioral therapy, and combination therapy in the treatment of ADHD

### Protocol:

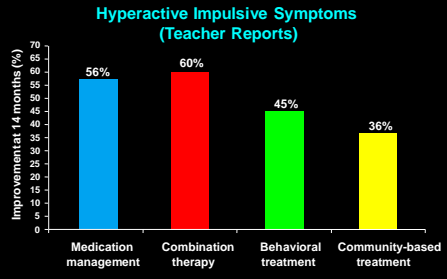
- Population: 579 children with ADHD combined type, aged 7-9.9 years
- In a 4-group parallel design, children randomly assigned to:
  - Medication alone (primarily methylphenidate)
  - Behavioral therapy alone
  - Combination of medication and behavioral treatment
  - Routine community care (medication and behavioral treatment)
- Duration of study treatment: 14 months

The MTA Cooperative Group. *Arch Gen Psychiatry*. 1999;56:1073-1086.

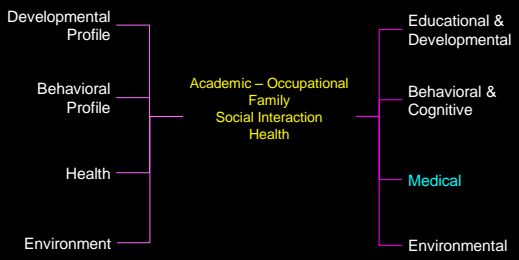
# MTA Study: Treatment Outcome: Teacher-Rated Inattention



# Long-term Outcomes of Therapies for ADHD in the MTA Study



# The Developmental Web



# American Academy of Pediatrics: Guidelines for the Treatment of ADHD

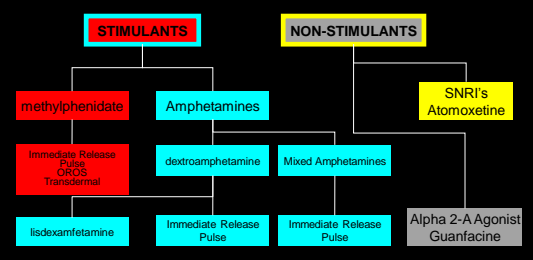
- Establish a treatment program that recognizes ADHD as a chronic condition
- Specify appropriate target outcomes to guide management
- Prescribe stimulant medication and/or behavior therapy to improve target outcomes in children with ADHD
- **If the treatment program has not met target outcomes, evaluate:**
  - Original diagnosis
  - Use of all appropriate treatments
  - Adherence to the treatment plan
  - Presence of coexisting conditions
- Using information from parents, teachers, and the child, follow-up to evaluate target outcomes and adverse effects

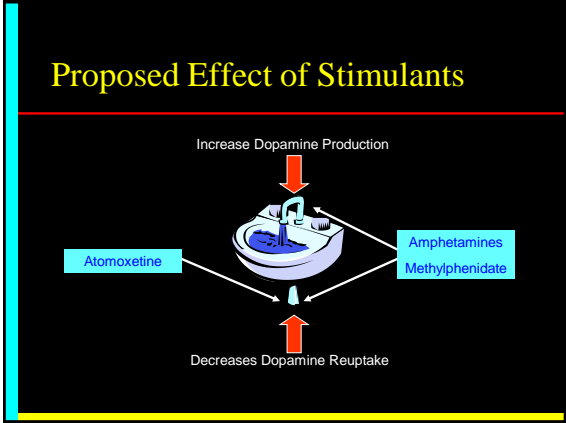
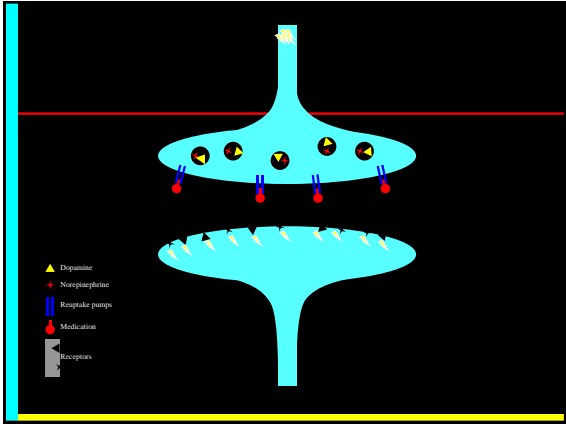
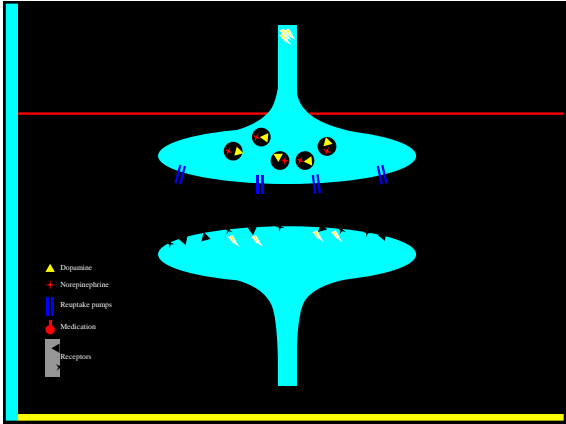
AAP. Pediatrics. 2001;108:1033-1044.

# Medications for Management of ADHD

- Stimulants
  - Methylphenidate products
  - Amphetamine salts
    - Mixed amphetamine salts
    - Dextroamphetamine sulphate
- SNRI's
  - Atomoxetine hydrochloride

# ADHD Medications





- ### Medications: Clinical Impact
- Increase control of attention
  - Increase impulse control
  - Decrease activity
  - Decrease disruptive behavior
  - Improve handwriting (in 50%)

- ### Medications: Clinical Impact
- Academic
  - Behavior
  - Socialization
  - Increase Production
  - Increase Compliance
  - Decrease Disruption
  - Increase Awareness

- ### Stimulant Medications
- Side Effects
    - Insomnia (50-60%)
    - Anorexia (50-60%)
    - Irritability (30%)
    - Headache
    - Stomachache
    - Nausea
    - Tics

## Atomoxetine: Side Effects

- Anorexia
- Dizziness - Sleepiness
- Dyspepsia
- Dermatitis
- Constipation
- Mood Swings
- *Transient elevation of liver enzymes*
- *Increased suicidality*

## Guanfacine: Side Effects

- Sleepiness, tiredness, drowsiness
- Constipation
- Low blood pressure
- Low heart rate
- Fainting
- Nausea
- Stomach aches
- Headaches
- Decreased appetite
- Nausea

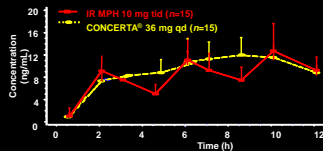
## Medications: Duration of Action

- Short Acting: 4 hours
- Intermediate Acting: 6 – 8 hours
- Long Acting: 8 – 12 hours  
24 hours

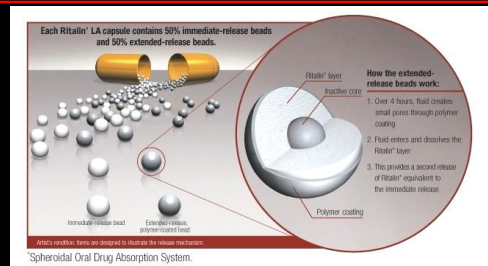
## Medications

- Short-Acting
  - Ritalin, Dexedrine, DextroStat, Focalin Methylin (Tablet, Chewable & Liquid)
- Intermediate-Acting
  - Ritalin SR, Metadate ER, Adderall, Ritalin LA, Metadate-CD, Methylin ER, Focalin XR
- Long-Acting
  - Dexedrine Spansules, Cylert, Adderall-XR, Concerta, Daytrana
- 24 hours
  - Strattera, Intuniv

## MPH OROS (Concerta®)

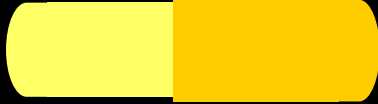
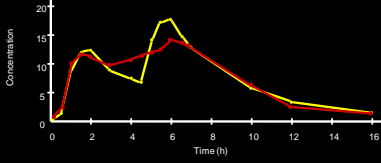


## MPH SODAS™ (Ritalin® LA) Pulse Release



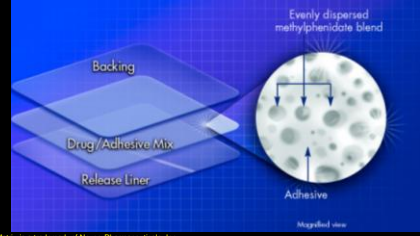
SODAS™ is a trademark of Elan Corporation, Plc

### Pulse Delivery System (SODAS, Difucaps)



### Daytrana DOT Matrix™ Transdermal Technology

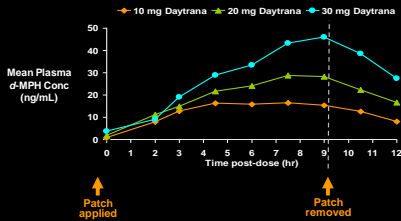
- Methylphenidate is mixed with adhesive



DOT Matrix is a trademark of Noven Pharmaceuticals, Inc.

### Pharmacokinetics with Daytrana

Mean Plasma Concentration of *d*-methylphenidate



Lower limit of quantification 0.25 ng/mL.

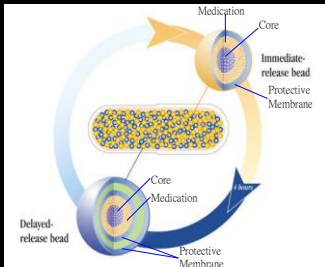
Pierce et al. Poster presented at the AACAP Annual Meeting, Toronto, October 20, 2005.

### Application and Removal/Disposal



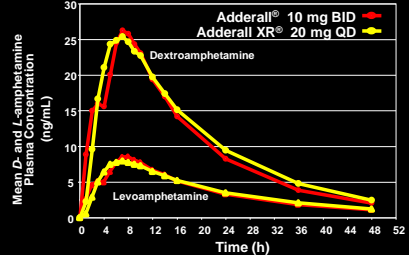
- Holding the patch down, the rest of the liner should be removed slowly and the exposed half should be pressed against the skin
- The patch should be pressed down with the palm of the hand for 30 seconds
- Upon removal, the patch should be folded in half, with sticky sides together, and discarded immediately in toilet or lidded container

### Pulse Delivery System for Adderall® XR and Metadate® CD



### Mixed Amphetamine Salts (Adderall XR®) Formulation Study

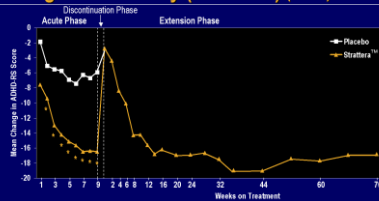
Bioequivalence of Adderall XR® 20 mg QD to Adderall® 10 mg BID



Tulloch et al. Pharmacotherapy 2002;22:1405.

## Atomoxetine (Strattera™) Efficacy

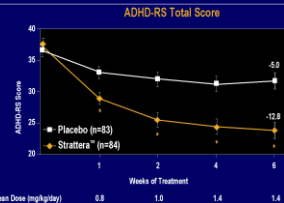
### Long-Term Efficacy (76 Weeks) (cont.)



\*p < .01 for Strattera vs placebo.  
\*\*p < .001 for Strattera within-group change.  
Spencer T, et al. Manuscript in preparation.

## Atomoxetine: Efficacy (Clinician)

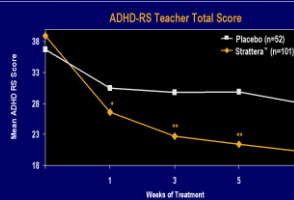
### Once-Daily Efficacy (cont.)



\*p < .05 vs placebo.  
Michelson D, et al. Am J Psychiatry. 2002;159(11):1886-1901.

## Atomoxetine: Efficacy (School)

### Once-Daily Efficacy: School Setting (cont.)



\*p < .05, \*\*p < .001.  
Allen AJ, et al. Manuscript in preparation.

## Behavioral Management

*What to do at Home*

## Core Principles for Behavior Management

- Immediacy of Consequences
- Frequency of Consequences
- Saliency of Consequences
- Frequent Changes in Rewards
- Act, Don't Yack
- Positives Before Negatives
- Anticipate Problems
- Pick Your Fights - Prioritize
- Expect Variability
- Practice Forgiveness

*It is not your fault...*

*But it is your problem*