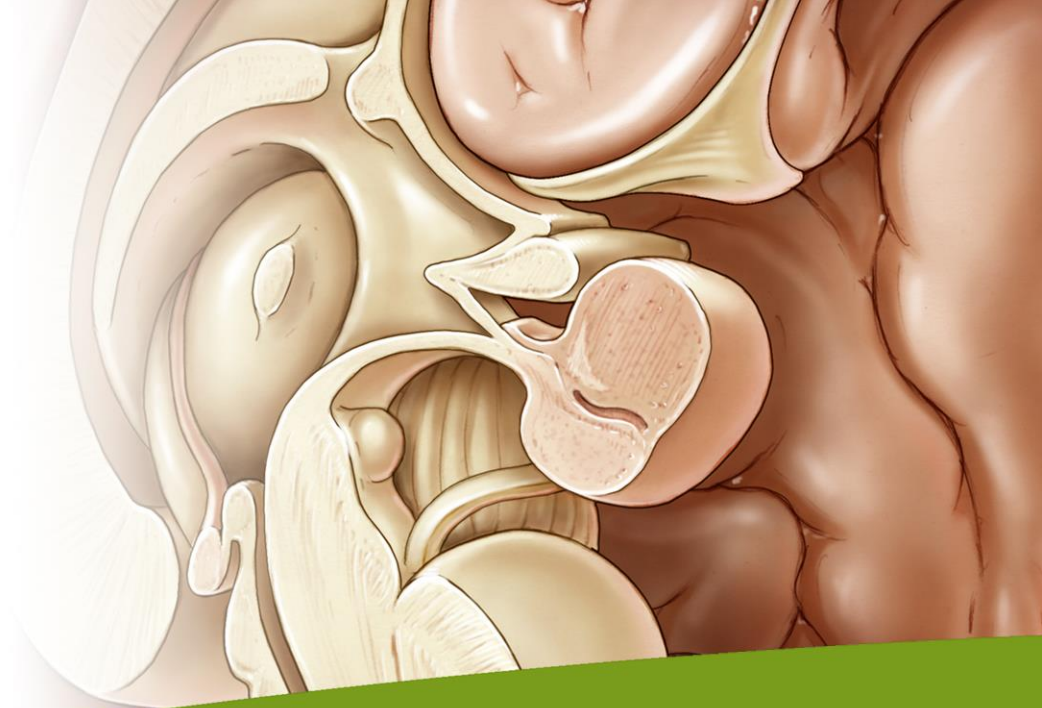


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# **Development of a screening tool differentiating patient symptoms in Cushing's, polycystic ovarian and metabolic syndromes**

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# DISCLOSURES

- Consultation:
  - Chiasma Inc.
  - Ipsen Biopharmaceuticals.
  - Novartis Pharmaceuticals Corporation
  - Nothing with respect to this presentation

## Diagnostic Dilemma



# Patient Presenting Symptoms: All patients

- Weight gain / difficulty with weight loss
- Fatigue
- Blurry vision
- Polyuria and polydipsia
- Hirsutism
- Amenorrhea / hypogonadism / Infertility



# Presenting Signs:

- Hypertension
- Increased: BMI  $>30$
- Midsection weight
- Facial rounding
- Dorsocervical hump
- Hyperglycemia: Diabetes Mellitus type 11
- Fatty liver
- Hyperlipidemia

# THE CLINICAL PROBLEM:

- Differential diagnosis
- Timely vs delayed diagnosis
- Appropriate efficacious treatment

# Differential Diagnoses:

- Metabolic Syndrome
- Polycystic Ovarian Disease
- Cushing's Disease

# Metabolic Syndrome: Defined

Any 3 of 5 risk factors:

Insulin resistance	Fasting glucose > 100mg/dL
Obesity: Increased waist circumference	( $\geq 30.00$ ) Male > 90cm (36inches) Female >80cm ( 32 inches)
Dyslipidemia: High Triglycerides Low HDL	triglycerides >150 mg/dL HDL <40mg/dL Males <50mg/dL Females
Hypertension	B/P > 130/85 >140/90

(Alberti et al., 2009)



# Polycystic Ovarian Disease (PCOS) : Defined

- An endocrine disorder involving:
  - Infertility/ irregular menses
  - Hyperandrogenism / hirsutism
  - Insulin resistance/ Diabetes Mellitus 11
  - Weight gain
  - in women with or without polycystic ovaries on imaging

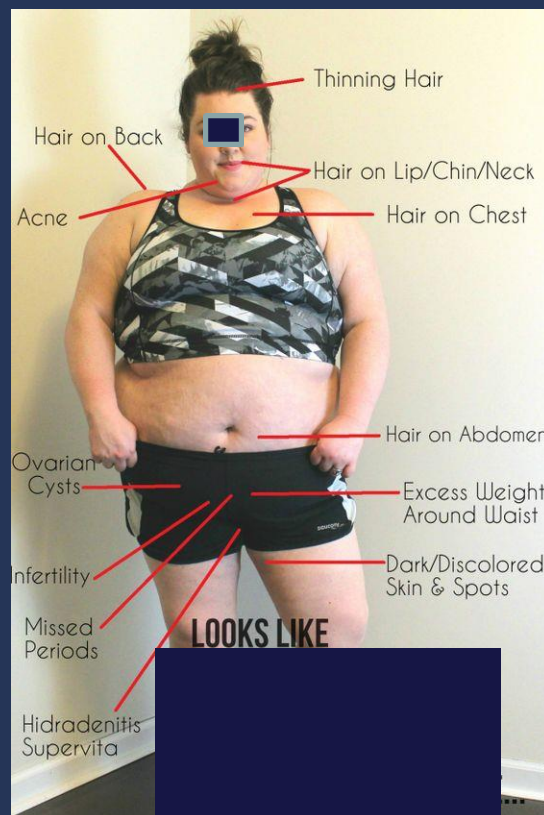
(Legro et al., 2013; Dunaif et al., 1992 ).

# Cushing's Syndrome: Defined

- Abnormal weight gain
- A fatty dorsocervical hump
- Facial rounded
- Hypertension
- type 2 diabetes
- Abdominal striae (may be pink/purple)

# Differential Treatment Modalities:

- Cushing's Syndrome:
  - Adrenalectomy ( unilateral)
  - Pituitary adonectomy
- Metabolic Syndrome
  - Lifestyle changes, diet and exercises
- Polycystic Ovarian Disease ( PCOS)
  - Low androgenic birth control
  - Treatment of insulin resistance



## AIM

1. To identify sentinel, patient reported symptoms and/or functional limitations that have a high specificity for CS vs metabolic syndrome (MS) or PCOS.
2. To develop a valid and reliable screening tool and scoring guide for use in primary care settings indicating the need for specialty referral.



## Method:

- A 205 item questionnaire
- Prospectively administered at patient presentation
- Symptoms and perceived dysfunction
- Progressive severity: 6 point Likert scale (0-5)
- Patients divided into 3 groups: CS, MS, PCOS
- Control group was solicited from community

# Analysis:

- Item analysis: questions reliability
- Difference between groups: ANOVA, Tamhane's post hoc analysis
- ROC analysis sensitivity and specificity for each diagnosis using PSAW 18.

# Questionnaire

- Modified scales:
  - Beck Depression Inventory
  - Eysenck Personality scale
  - Epworth Sleepiness Scale
  - Krupp Fatigue Severity Scale
  - Functional Assessment Rating Scale
  - Symptoms of pituitary diseases derived from review of literature and patient interviews.

# Cushing's Syndrome Screening Tool (CSST)

**205 Items**

item analysis  
n=127

**56 Items**

Cronbach's' Alpha =0.97

**10 Items**

**CS vs MS vs PCOS**

p=>0.05

# Cushing's Syndrome Screening Tool (CSST)

	I have:	Not at all					Severe
1	Facial flushing or redness	0	1	2	3	4	5
2	A hump on the back of my neck	0	1	2	3	4	5
3	Larger than usual breasts (males and Females)	0	1	2	3	4	5
4	Dry/coarse skin	0	1	2	3	4	5
5	Easy sweating /body odor	0	1	2	3	4	5
6	Dark pink/purple stretch marks on body/abdomen	0	1	2	3	4	5
7	Increasing facial rounding	0	1	2	3	4	5
8	Persistent Hunger	0	1	2	3	4	5
9	Swelling in feet and ankles	0	1	2	3	4	5
10	Fatigue that disrupts my life /work life	0	1	2	3	4	5
<b>TOTALS</b>		<b>0</b>	<b>10</b>	<b>20</b>	<b>30</b>	<b>40</b>	<b>50</b>



**N = 56    Groups:**

- 1: Cushing's syndrome
- 2: metabolic syndrome (MS)
- 3: PCOS
- 4: Healthy controls solicited from community volunteers.

## Inclusion Criteria:

- Biochemical/pathology confirmed diagnosis of Cushing's syndrome/disease
- Patients with Non-functioning adenomas or no pituitary or adrenal adenoma meeting criteria for PCOS and MS
- Healthy controls: No comorbidities/tumor

## Exclusion Criteria:

- Unstable co-morbidities
- New treatments within 6 months of presentation
- A significant life stressor within 12 months of presentation
- Prior pituitary or adrenal surgery

# Results: n= 56    14 males / 33 females

## Group 1

- CUSHINGS SYNDROME ( CS) n=14
- (3Male/11Female)

## Group 2

- METABLOIC SYNDROME (MS) n=10
- (3Male /7Female)

## Group 3

- POLYCYSTIC OVARIAN DISEASE (PCOS) n=11
- (11 Females)

## Group 4

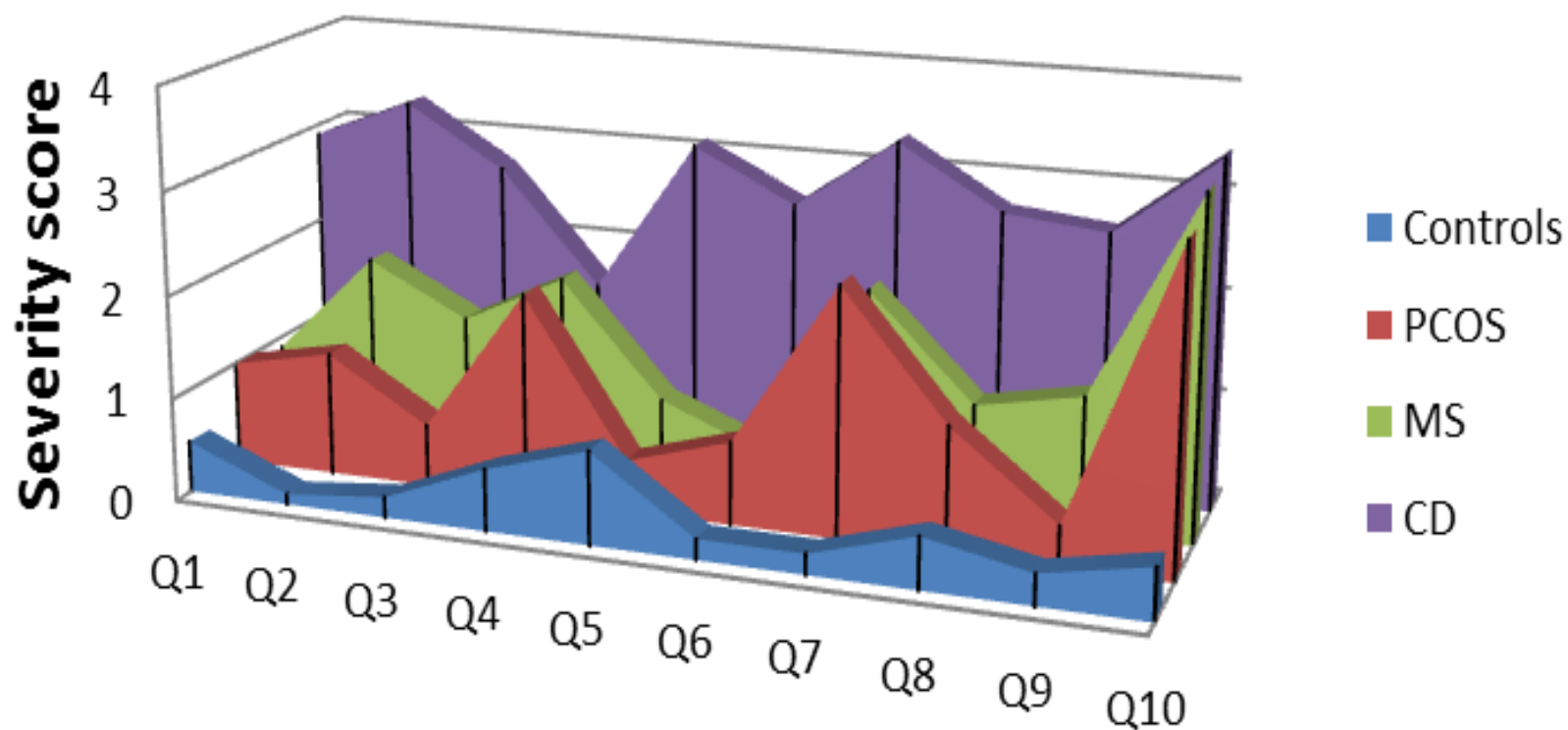
- CONTROLS n=21
- (8 Males/13 Females)

# Results:

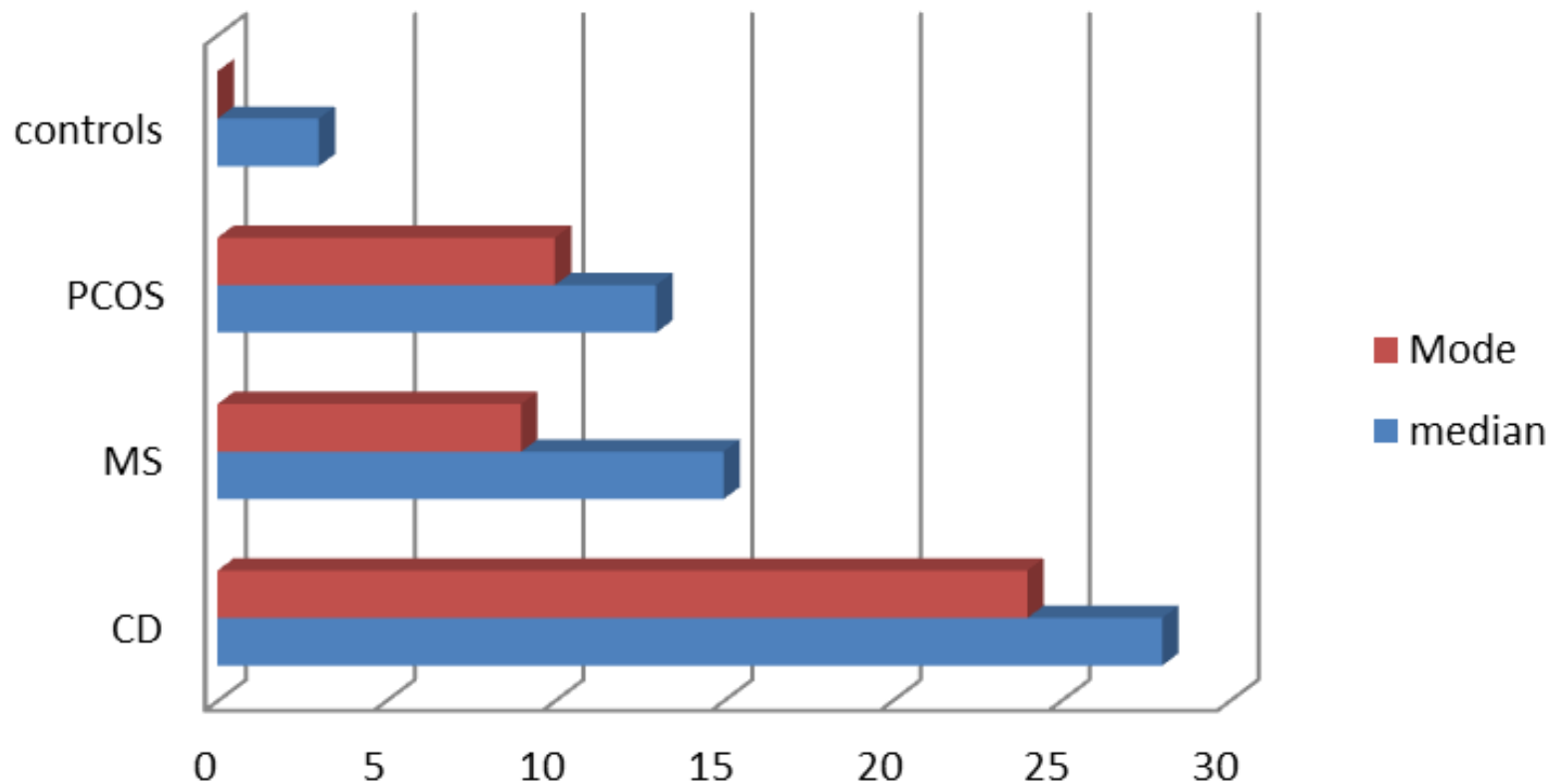
	Group 1: CS	Group 2: MS	Group 3: PCOS	Group 4: Control	P value
<b>N= 56</b>	14	10	11	21	
<b>Mean Age</b>	41	52	30.6	40.6	0.004 *PCOS
<b>Gender</b>	3M/11F	3M/7F	11 F	8M/13	0.01 Females
<b>BMI</b>	37.4	38.3	31	26.7	0.000 (controls)
<b>Mean severity Scores ( 50)</b>	28.2 (5-48)	15.1 (5-25)	13.3 (7-20)	3.7 (0-10)	0.000 CS
<b>Hyperlipidemia</b>	4 (28.6%)	9 (90%)	0	0	p>0.001 MS
<b>Insulin resistance</b>	12(85.7%)	9 (90%)	4 (36.3%)	0	P>0.001 MS/CS
<b>HTN</b>	12(85.7%)	8 (80%)	2 (18%)	1	P>0.001 MS/CS



# Question Severity Score by Diagnosis



## Diagnostic Discriminating Score



# Cushing's Syndrome Screening Tool (CSST)

- 10 items Cronbach's  $\alpha = .95$
- Sensitivity = 85.7%
- Specificity = 97% (AUC= 0.965)

## Conclusion:

- In study context, tool demonstrates high item reliability, sensitivity and specificity for CS.
- Did not help to differential MS from PCOS.
- CCST needs further validation in broader population.
- May be useful for differentiating patient with Cushing's syndrome from those with both Metabolic Syndrome and Polycystic Ovarian Disease in primary care setting.

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A scenic view of a city at sunset. In the foreground, a cable car is suspended from cables, moving across the frame. The background shows a city with a river, buildings, and mountains under a colorful sky.

Thank you.

Questions?

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