AUTUMN MEETING

Hotel Russell, London

11th November 2011

Gold sponsors:

Can we improve outcomes in thyroid eye disease?

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Cardiff University School of Medicine

Thyroid Eye Disease

In Graves' disease

- 5% Severe TED
- 20-50% clinical TED
- 70-90% CT detectable TED

Relatively more common in men and smokers

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Manifestations of thyroid eye disease

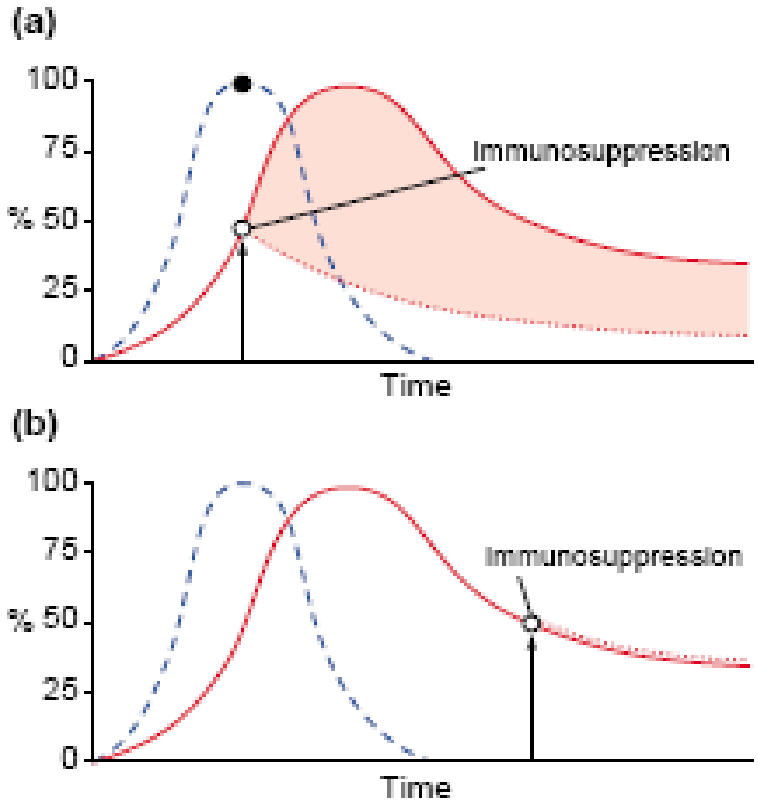
1. **Soft tissue signs**, chemosis, periobital oedema
2. **Proptosis**
3. **Diplopia**/ abnormal EOM function esp restricted upgaze
4. **Optic neuropathy**

CAN ALL OCCUR SEPARATELY

Usually Asymmetrical, 15% unilateral

10% euthyroid

Natural Hx: Active versus inactive disease



Differential diagnosis

- Myasthenia gravis
- Orbital myositis (swollen eye muscle)
- (retroorbital tumour)
- "…..allergic conjunctivis"

Active versus inactive disease

- Active

- Inactive

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University of BRISTOL

NATIONAL EYE RESEARCH CENTRE
Registered Charity No. 294087

ABOVE & BEYOND

Amsterdam Declaration Oct 2009

- Graves' orbitopathy affects hundreds of thousands of people in the world every year. It causes pain, discomfort, double vision, disfigurement and sometimes blindness. People suffering with Graves' orbitopathy have a poor quality of life and long-term psychosocial morbidity. The quality of care received by the majority of people affected by this condition can be improved.
- Conventional treatments are effective when used appropriately and by centres with expertise.
- Not all patients are offered effective treatments either because most are not referred early or not at all.
- People at high risk of developing Graves' orbitopathy can be identified and effective risk management can potentially lessen the severity of the disease.

TEAMeD

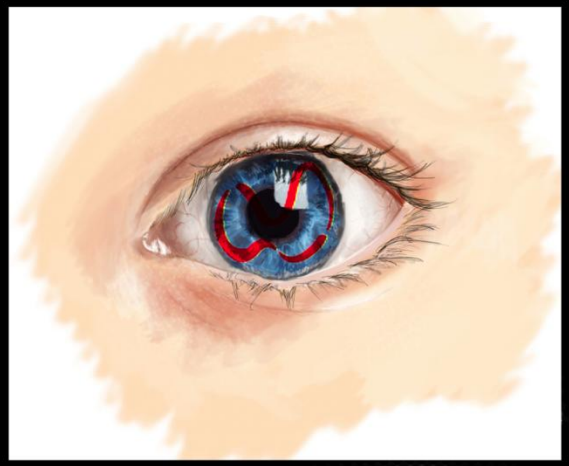
Thyroid Eye Disease Amsterdam Declaration Implementation Group UK

The Amsterdam Declaration on Graves' Orbitopathy: Improving Outcomes for Thyroid Eye Disease has been signed by over 87 representatives of patient and professional organisations since the 10th International Symposium on Graves' Orbitopathy in Amsterdam on 30 October 2009

Working together to

- **RAISE AWARENESS** amongst patients, the public and health care providers via:
  - Awareness campaign
  - Publications
  - Patient tool for symptom recognition

- **ESTABLISH PATHWAYS** for referral and care:
  - Develop guidelines



- **IMPROVE PATIENT LIVES** by improving access to:
  - Information
  - Early diagnosis
  - Timely and appropriate treatment
  - Skilled professionals
  - Joint care from endocrinologists and ophthalmologists

- **REDUCE IMPACT OF DISEASE** by disseminating information on:
  - Endocrine management
  - Radioactive iodine advice
  - Smoking risks

- **ASSURE QUALITY OF CARE** by developing audit tools for TED:
  - Patients' experience of care pathways
  - Endocrine management of TED

British Thyroid Foundation (Registered Charity No. 1006191)

TEDct (Registered Charity No: 1095967)

British OculoPlastic Surgery Society

British Thyroid Association

Society for Endocrinology

Scottish Ophthalmological Club

The Royal College of Ophthalmologists

Royal College of Physicians

Improving outcomes

1. Prevention
2. Effective Treatment
3. Early referral for specialist assessment and treatment

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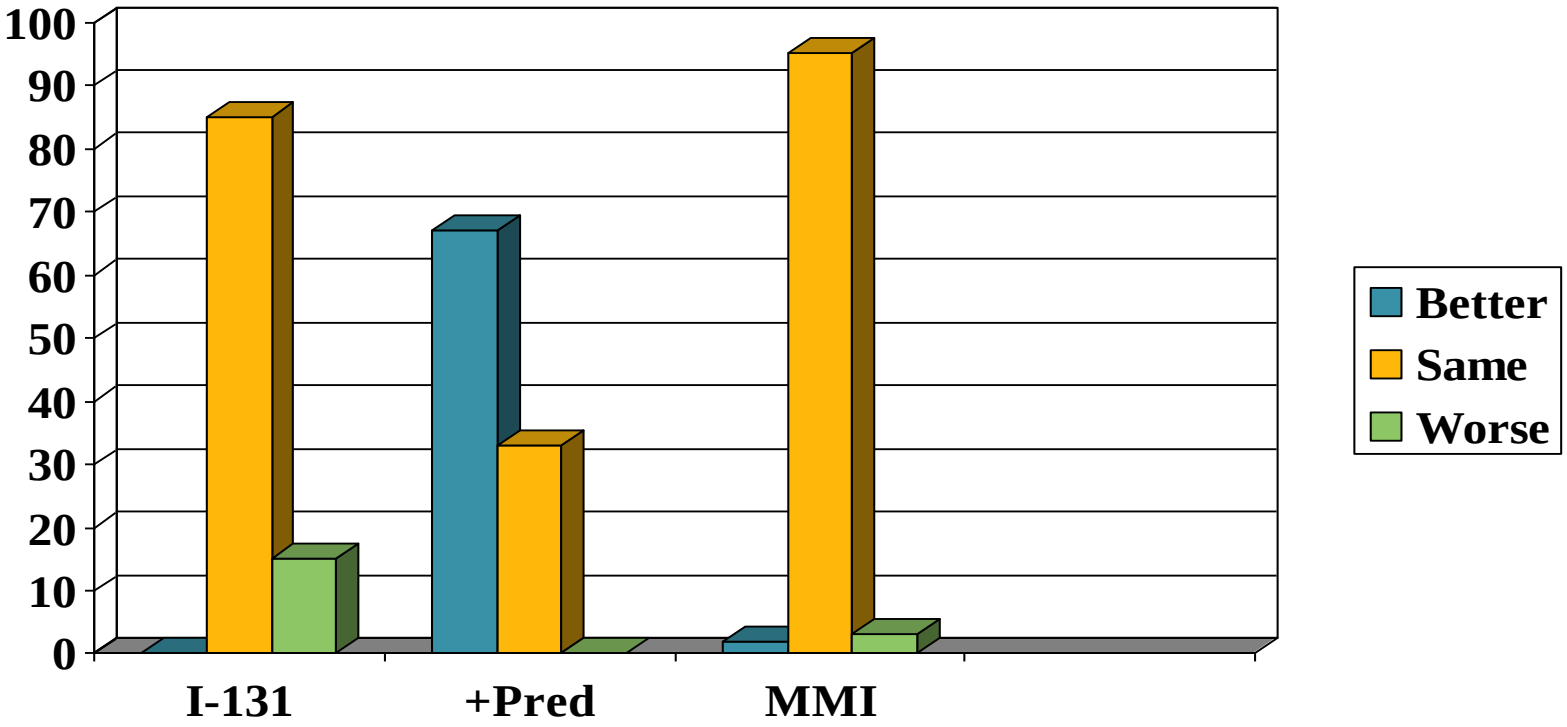
PREVENTION: Reducing the risk and severity of TED

- Treat thyrotoxicosis
- Avoid I-131 (in the active phase)
- Stop smoking

I – 131 and TED



Bartelena et al 1998

Lai et al 2010: 0.2mg/kg or 6 wks sufficient

TSHR antibodies and treatment

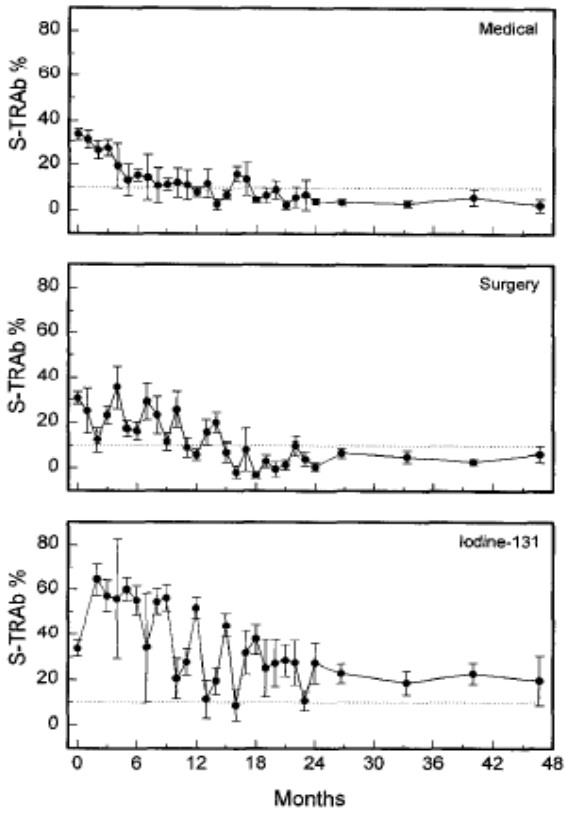


FIG. 2. The serum concentration of TRab during the first 4 yr in the different treatment groups. See also Fig. 1.

Torring et al
1996

Smoking

- Increase risk of developing TED
- Reduces response to therapy
- Increase requirement for strabismus surgery

Improving outcomes

1. Prevention
2. **Effective Treatment**
3. Early referral for specialist assessment and treatment

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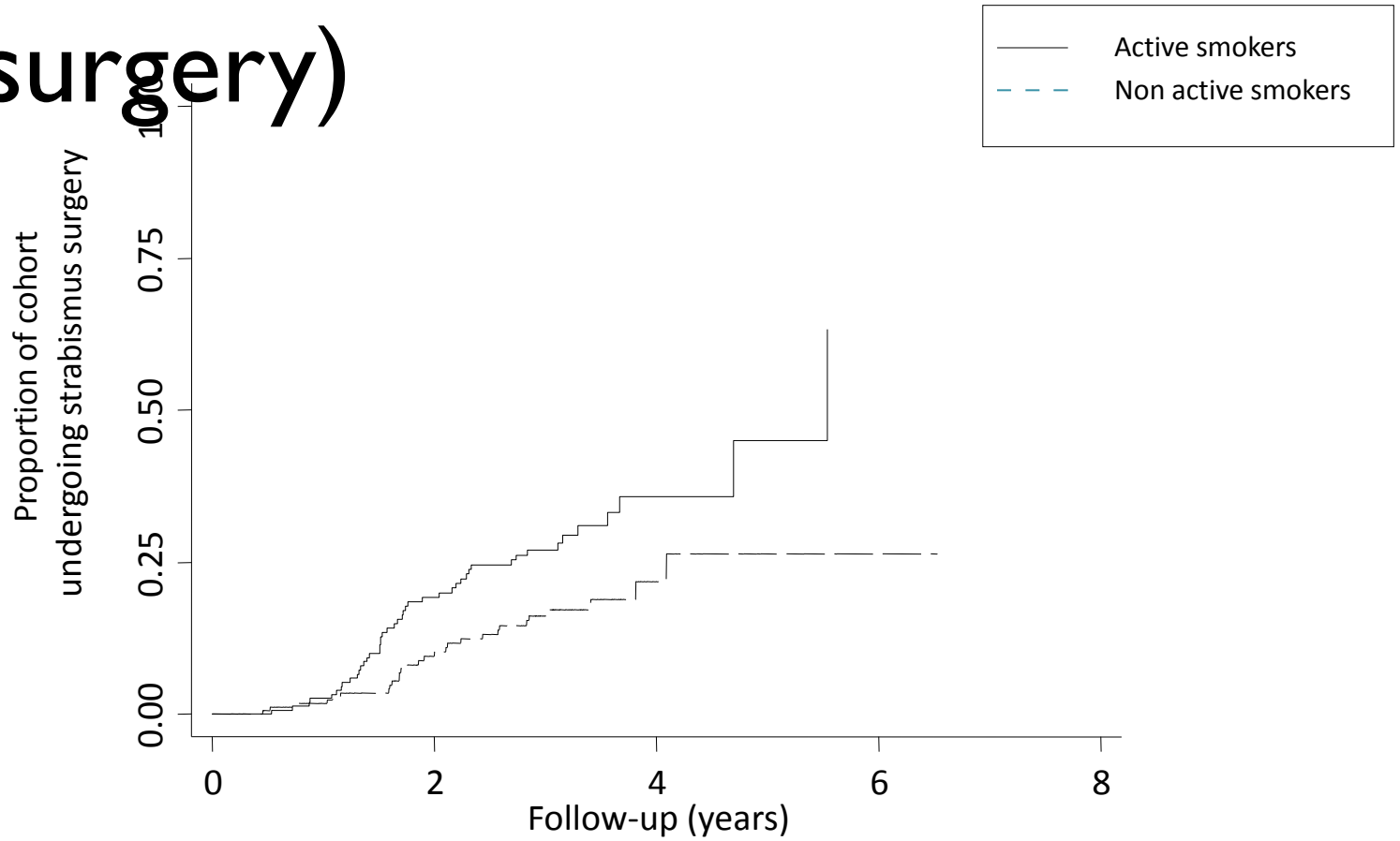
Smoking (& Strabismus surgery)



Number at risk

Non active smokers	192	126	20	4	3
Active smokers	165	108	17	2	2

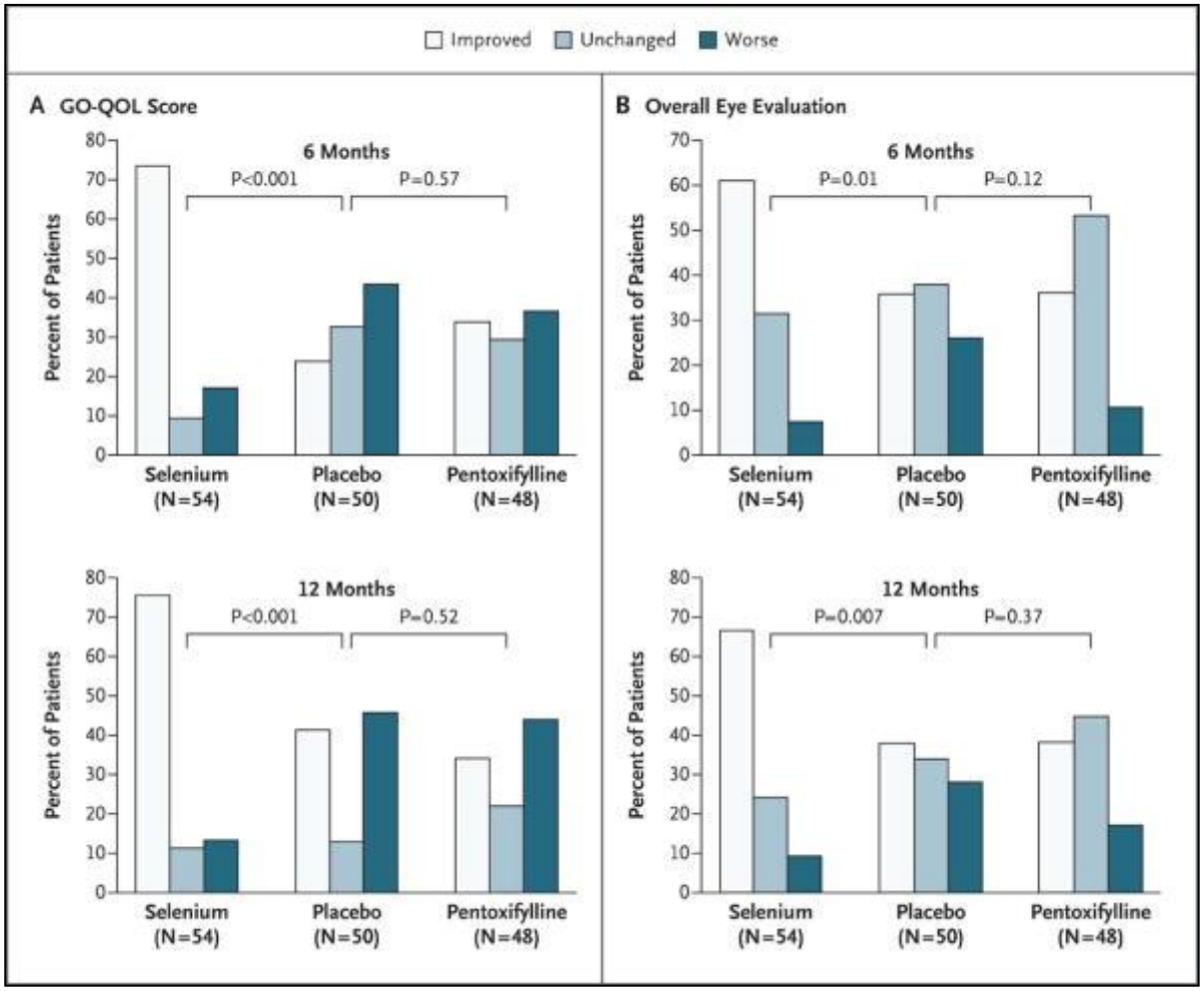
Figure 2. Proportion of cohort undergoing strabismus surgery according to smoking status at presentation

Rajendram et al 2011

Treatments for TED

- Local
- Systemic
  - Selenium
  - Steroids – p.o., i/v
  - DXT
  - Other immunosuppressants – CyA, Ritux
- Surgical
  - Decompression
  - Strabismus
  - Oculoplastic

Marcocci et al 2011 - Selenium



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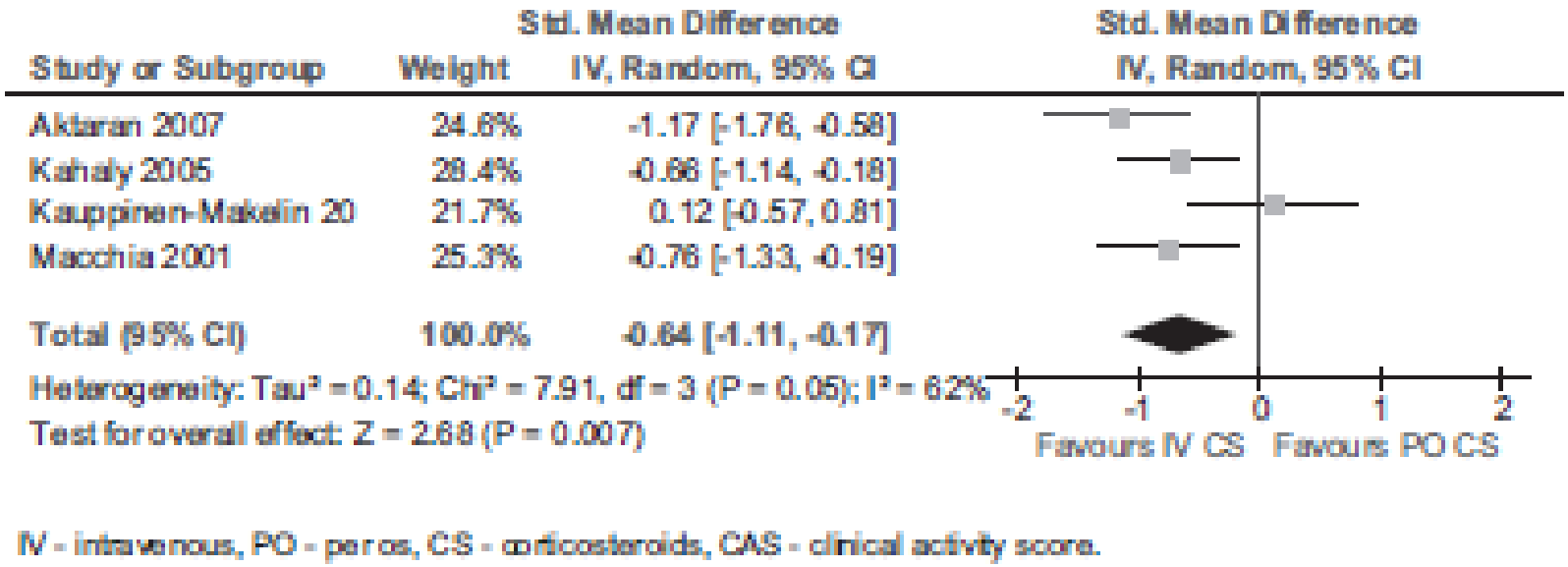
Selenium

- Marcocci et al used 100mcg bd o sodium selenite = 105 mcg of elemental selenium
- Lambert selenium = 200mcg – use ½ tablet daily.

Stiebel-Kalish et al metanalysis 2009: iv vs po steroids



IV - intravenous, PO - per os, CS - corticosteroids, CAS - clinical activity score.

FIG. 2. Intravenous corticosteroids *vs.* oral corticosteroids. The outcome was CAS at the end of follow-up. PO, Per os; CS, corticosteroids.

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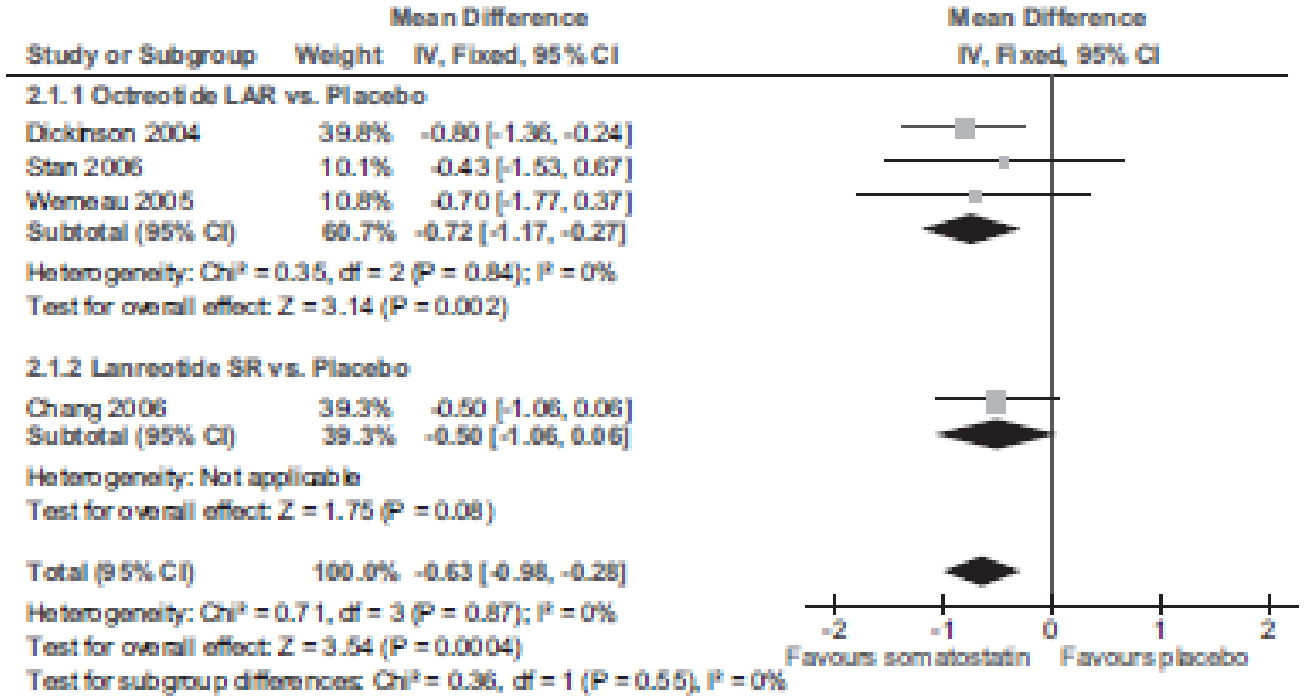
Stiebel-Kalish et al metanalysis 2009: somatostatin analogues



CAS – clinical activity score, LAR – long actin release, SR – slow release

FIG. 3. Somatostatin analogs *vs.* placebo. The outcome was CAS at the end of follow-up.

Stiebel-Kalish et al metanalysis 2009: orbital DXT

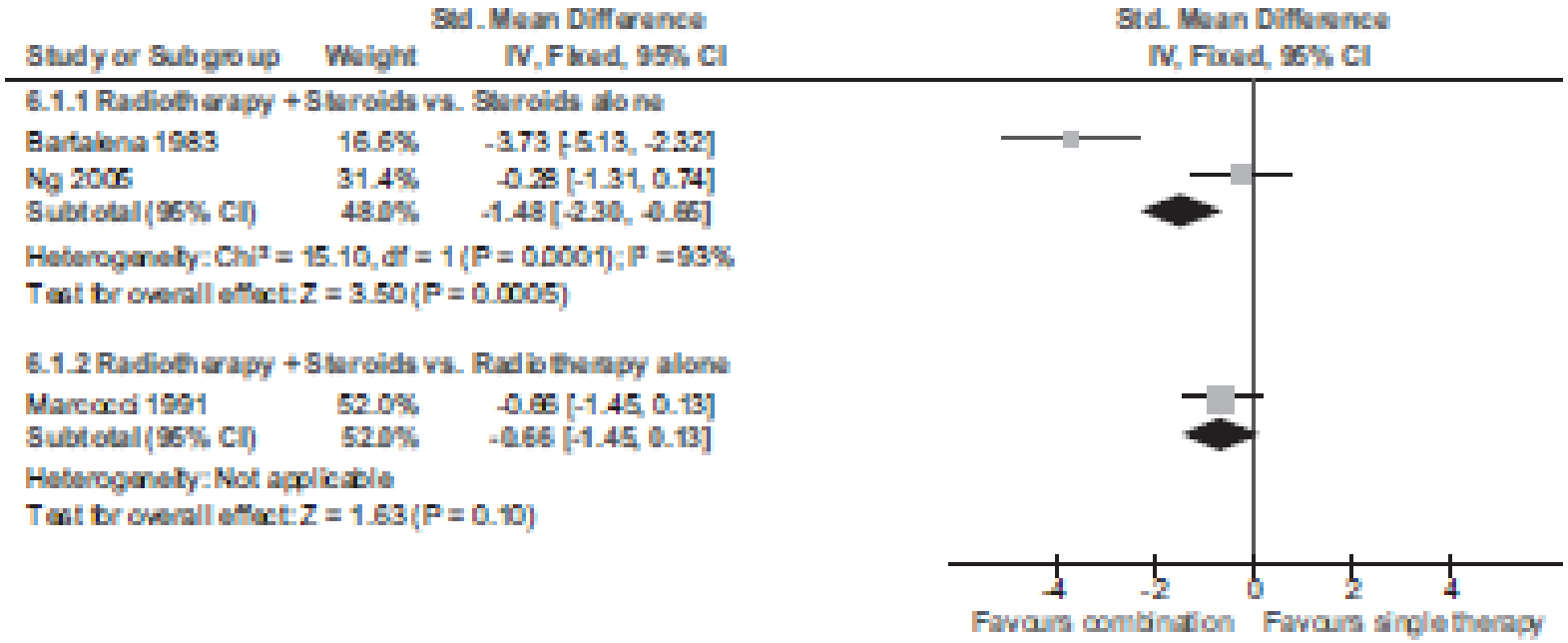


FIG. 4. Orbital radiotherapy plus corticosteroids *vs.* either treatment alone. The outcome was OI/TES at the end of follow-up.

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Stiebel-Kalish et al metanalysis 2009: other treatments

- Total thyroidectomy not better then subtotal
- Steroids better than ciclosporin but Ciclosporin + steroids better.

Dysthyroid Optic Neuropathy

- Suspect if any change in vision/red desaturation:
  - Refer URGENTLY
  - Iv steroid or
  - Urgent decompression

Rituxumab

Patients (no.)/therapy	Weeks	Proptosis	*P* (ANOVA vs week 0)	CAS
GD (no. 2)/rituximab	0	19.0±0.7*	–	–
	8	18.0±1.2	NS	–
	20	17.7±1.1	NS	–
	30	17.3±0.9	<0.006	–
	P (ANOVA)	<0.003 vs TAO <0.015		
TAO (no. 7)/rituximab	0	22.4±0.5	–	4.7±0.5
	8	21.8±0.6	<0.02	2.7±0.3
	20	21.3±0.6	<0.02	2.0±0.4
	30	20.9±0.6	<0.005	1.8±0.8
	P (ANOVA)	<0.0001		<0.0001 vs Methylpred. <0.05
TAO (no. 20)/methylpred.	0	22.6±0.6	–	4.1±0.3
	8	22.3±0.6	NS	2.6±0.3
	20	21.9±0.6	<0.03	2.1±0.3
	30	22.1±0.6	NS	2.0±0.4
	P (ANOVA)	<0.014 vs Rituximab NS		<0.0001

*Mean ± S.E.M.

Salvi et al 2007

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Combination therapy

Cirted

Combined Immunosuppression and Radiotherapy in Thyroid Eye Disease Trial

Moorfields Eye Hospital NHS
NHS Foundation Trust

Thyroid Eye Disease Treatment Trial

Please refer patients who have:

- Retrobulbar pain
  (even if only on eye movement)
- Red eyes
- Eyelid swelling
- Conjunctival chemosis
- Recent onset or worsening diplopia
- Increasing proptosis

AND who:

- are aged between 20 and 75 years old
- are not pregnant or planning pregnancy
- are not diabetic (excluding steroid induced)

Please contact:

Miss Rathie Rajendram (CIRTED Research Fellow)
Mr Jimmy Uddin & Mr Geoff Rose
Moorfields Eye Hospital NHS Foundation Trust
Telephone No: 020 7253 3411 ext: 4246
Pager: 07699 747228
Email: CIRTED@moorfields.nhs.uk

www.cirted.org

University of BRISTOL

NATIONAL EYE RESEARCH CENTRE

Moorfields Eye Hospital NHS
NHS Foundation Trust

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Surgery in TED (usually in the inactive phase)

- Orbital surgery (decompression)
- Strabismus surgery
- Oculoplastic surgery

Improving outcomes

1. Prevention
2. Effective Treatment
3. **Early referral for specialist assessment and treatment**

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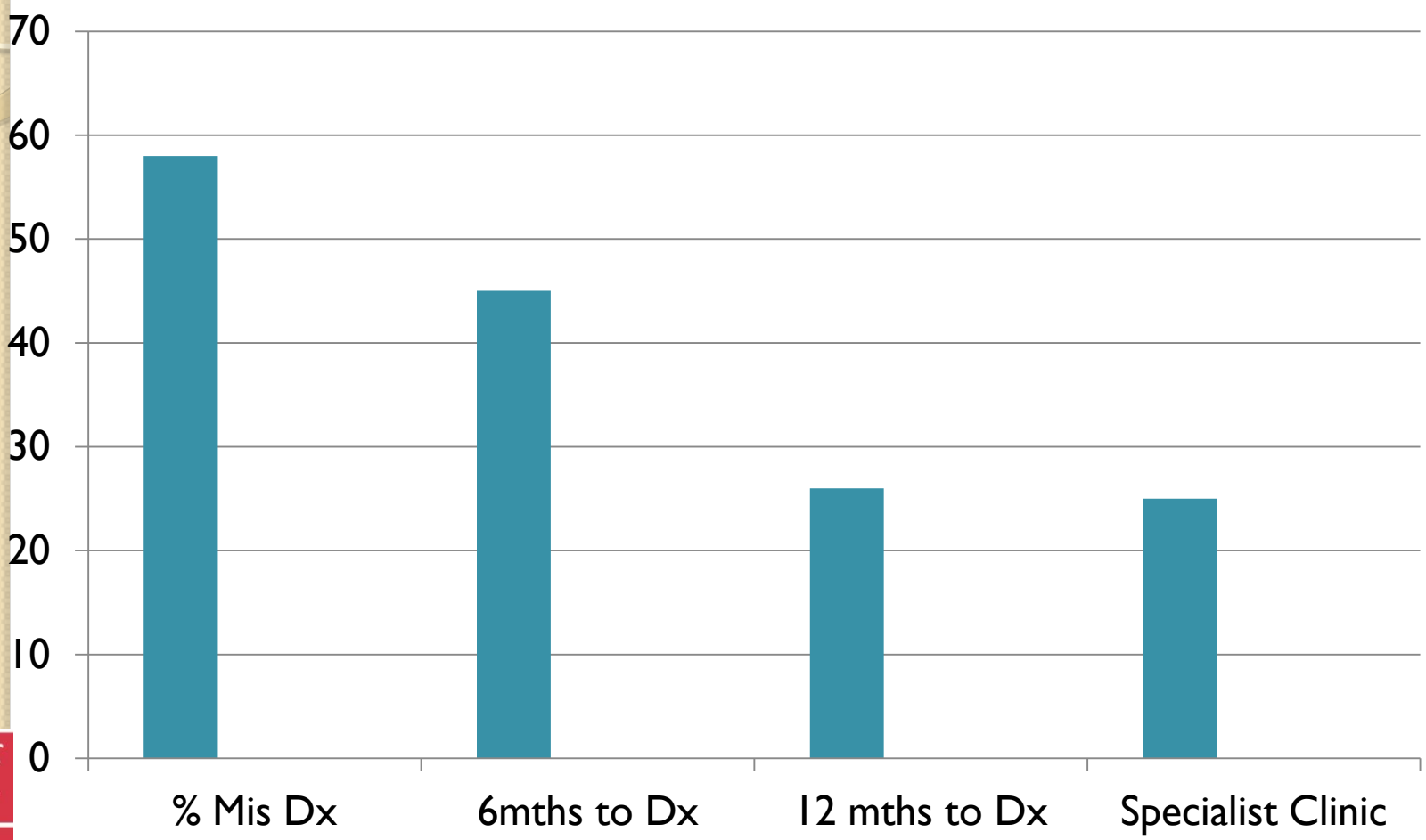
Access to care in TED



Estcourt et al 2009

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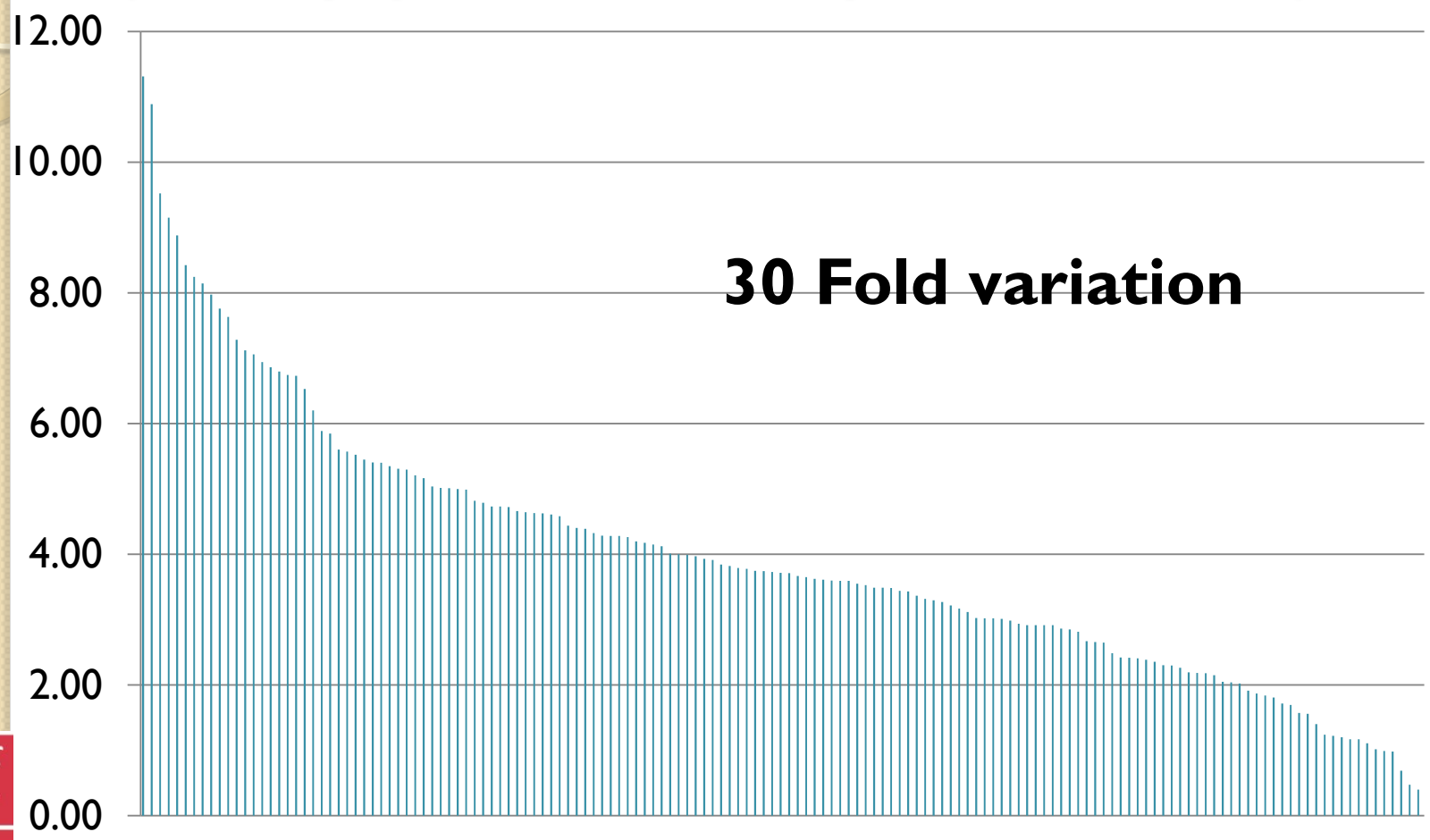
Decompression procedures by PCT (Yearly procedures per 100,000)



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Regional Variation in Specialist Care for TED

Decompressions /year	No. NHS Trusts
> 10	8
5-10	8
< 5	52

Reduce the impact on people's lives…..

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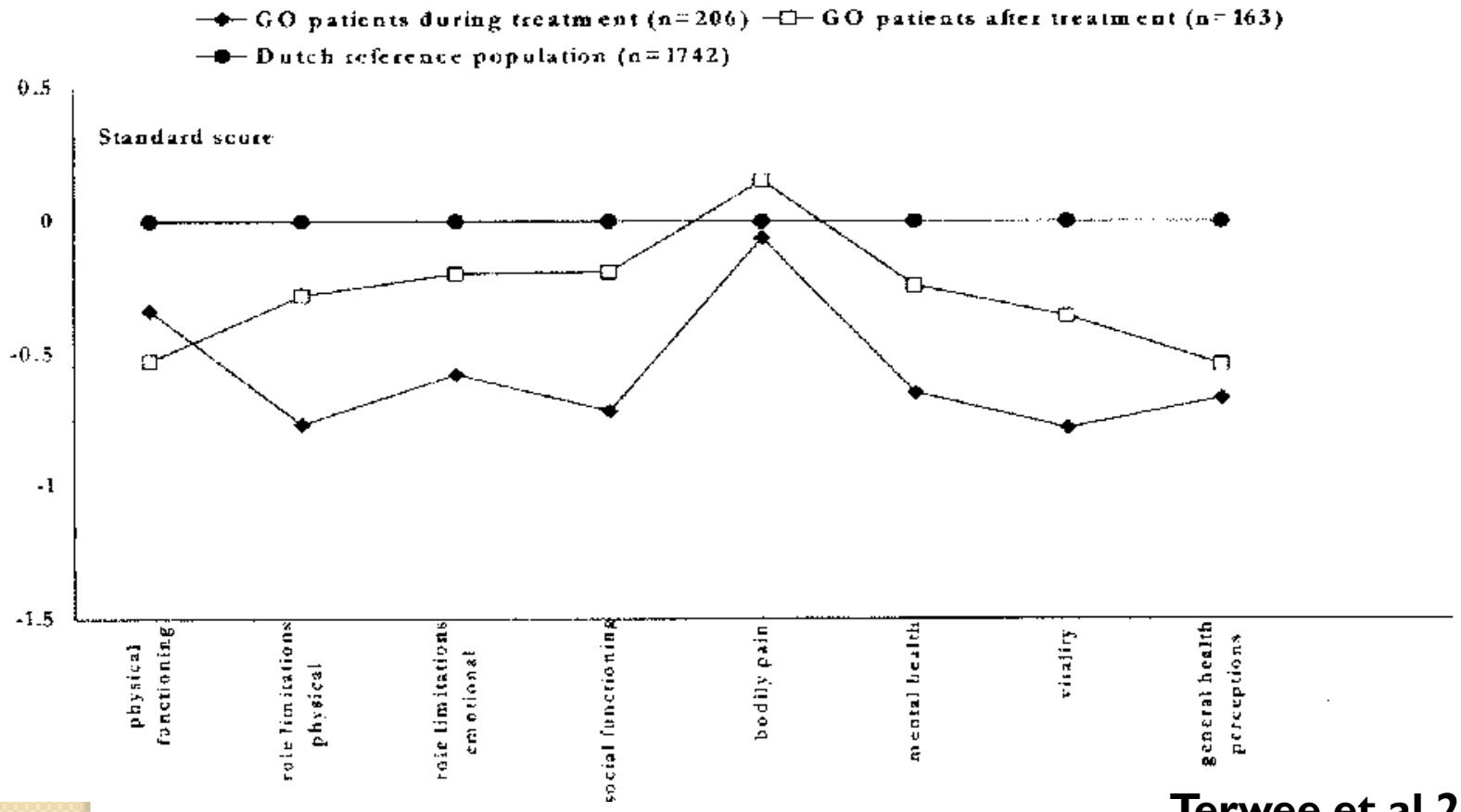
TED is very distressing to patients



Terwee et al 2002

TEDct

Charitable Trust

Thyroid Eye Disease Head Office

www,tedct.co.uk

Email: ted@tedct.co.uk

Summary

- Thyroid eye disease is easily missed and underestimated
- PREVENT: I-131, smoking, avoid hypothyroidism
- TREAT early: selenium, steroids and immunosuppression in active disease, rehabilitative surgery
- REFER promptly: to **specialist** centre.
- (Do not forget the psychological impact)

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