Association of British Clinical Diabetologists

Sandwell and West Birmingham Hospitals NHS
NHS Trust

Problems with the NICE guideline for exenatide exposed in the Association of British Clinical Diabetologists (ABCD) Nationwide Exenatide Audit

R.E.J. Ryder[1], K.Y. Thong[1], M.L. Cull[1], A.P. Mills[1], C. Walton[2], K.A. Adamson[3], D.S.Dove[4]
on behalf of the ABCD nationwide exenatide audit contributors

[1]Diabetes, City Hospital, Birmingham, United Kingdom, [2]Diabetes, Hull Royal Infirmary, Hull, United Kingdom,
[3]St John's Hospital, Livingston, United Kingdom, [4]Wexham Park Hospital, United Kingdom

Introduction

- According to the National Institute of Clinical Excellence (NICE), exenatide[1]:
  - use should be restricted to:
    - patients with HbA1c ≥ 7.5%
    - patients with BMI ≥ 35 kg/m² (or BMI < 35 kg/m² in certain ethnic groups) unless there was a professional hazard using insulin
    - third line therapy to metformin and sulfonlyurea
  - continuation should be restricted to those who achieve HbA1c reduction of ≥ 1% AND weight loss of ≥ 3% initial body weight at 6 months
- We examined the utility of this recommendations against results from the ABCD nationwide exenatide audit

Methods

- In the audit, 315 contributors from 126 centres submitted data on 6717 patients.
- Two groups of patients were analysed:
  - All patients with both HbA1c and weight at baseline and 6 months
  - Patients above but also who satisfy NICE patient selection guidelines ie. patients were excluded if:
    - HbA1c <7.5%
    - BMI <35 kg/m² (unless has occupational hazard using insulin)
    - on insulin
    - on triple oral therapy

Results

Effects on patient numbers

- 1882 patients had baseline and 6 month HbA1c and weight data
- 1081 patients had baseline and 6 month HbA1c and weight data, and also satisfy NICE criteria
  - The number of patients excluded by each NICE criteria is outlined in Table 1

Table 1: Effects of NICE guidelines on patient numbers and NICE criteria for treatment success

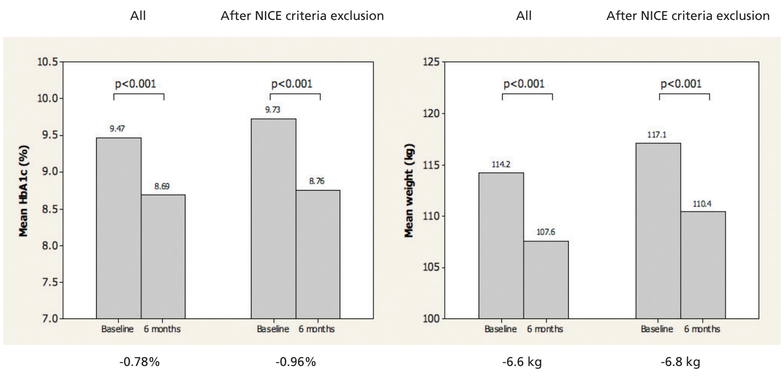
	N	Both HbA1c and weight success	HbA1c success only	Weight success only	Both fail
All patients with 6 month data	**1882**	**28.6%**	**16.3%**	**39.3%**	**15.8%**
Exclude HbA1c <7.5% only	1693	30.7%	18.1%	35.7%	15.4%
Exclude BMI <35 without occupational reason only	1638	28.6%	15.6%	39.9%	15.8%
Exclude patients on triple oral therapy only	1500	30.3%	17.8%	37.0%	14.9%
Exclude patients on triple oral therapy only	1780	28.7%	16.0	39.7	15.7
Exclude all 4 criteria together	**1081**	**32.9%**	**18.9%**	**34.0%**	**14.2%**

- Patient examples whereby NICE patient selection criteria appears problematic
  - Patient 1: **Baseline HbA1c of 7.1%** but achieved HbA1c reduction of 1.5% and 9kg weight loss
  - Patient 2: **BMI of 32** (Caucasian) but achieved HbA1c reduction of 2.5% and 6.9kg weight loss
  - Patient 3: **On long acting insulin** 180 units/day but achieved HbA1c reduction of 1.5% and 11 kg weight loss
  - Patient 4: **On triple oral therapy** but achieved HbA1c reduction of 1.2% and 8kg weight loss
- **Effects of NICE criteria on the frequency of successful treatment response**
- Any HbA1c or weight improvement
  - Among the 1882 patients, 89.2% had a weight reduction, 68.2% had HbA1c reduction, and 60.1% had a reduction in both.
  - Among the 1081 patients, 88.6% had a weight reduction, 72.1% had HbA1c reduction, and 63.4% had a reduction in both.
- NICE criteria for successful treatment response
  - Among the 1882 patients, 67.9% achieved weight loss criteria, 44.9% achieved the HbA1c criteria, only 28.6% achieved both
  - Among the 1081 patients, 66.9% achieved weight loss criteria, 51.8% achieved the HbA1c criteria, only 32.9% achieved both
- **Effects of NICE criteria on the frequency of successful treatment response**
- Not surprisingly, excluding patients using NICE criteria led to patients with higher mean baseline HbA1c, weight and BMI (Table 2)
- It also selected more patients who were Caucasian and with lower duration of diabetes
- Patients also achieved greater HbA1c and weight reduction (Fig. 1)

Table 2: Effects of NICE selection criteria on baseline characteristics of patients

	Patients before NICE criteria exclusion (n=1882)		Patients after NICE criteria exclusion (n=1081)		P value
	n		n		
Male %	1785	57.3	10.16	57.2	0.971
Caucasian %	1400	87.7	692	94.1	<0.001
Age (yrs)[a]	1757	55.3 (10.3)	991	55.0 (10.4)	0.512
Diabetes duration (yrs)[a]	1497	9.7 (5.8)	871	8.9 (5.4)	0.001
HbA1c (%)[a]	**1882**	**9.47 (1.67)**	**1081**	**9.74 (1.47)**	**<0.001**
Weight (kg)[a]	**1882**	**114.2 (22.9)**	**1081**	**117.1 (22.4)**	**0.001**
BMI (kg/m²)[a]	**1047**	**40.3 (8.2)**	**556**	**42.5 (6.5)**	**<0.001**

Figure 1: Effects of NICE selection criteria on HbA1c and weight reduction



Discordant HbA1c or weight response among individual patients

- There were many patients who achieved a substantial reduction in HbA1c but not weight and vice versa See Fig. 2,3,4,5

Figure 2: Examples of patients who respond predominantly to either HbA1c or weight

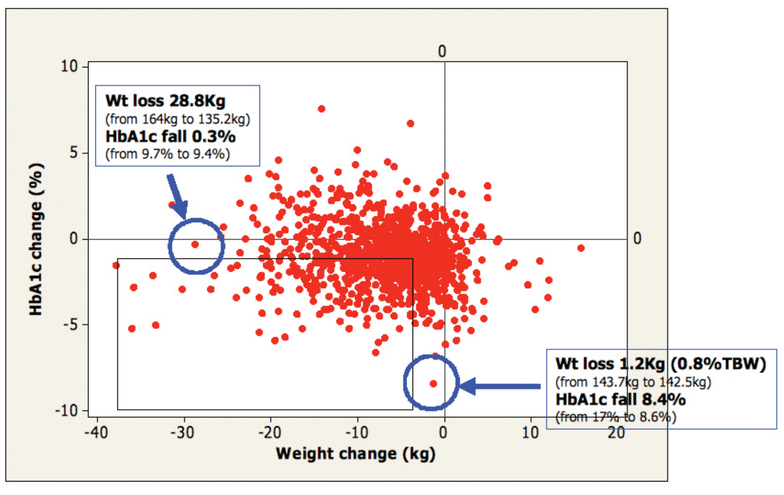
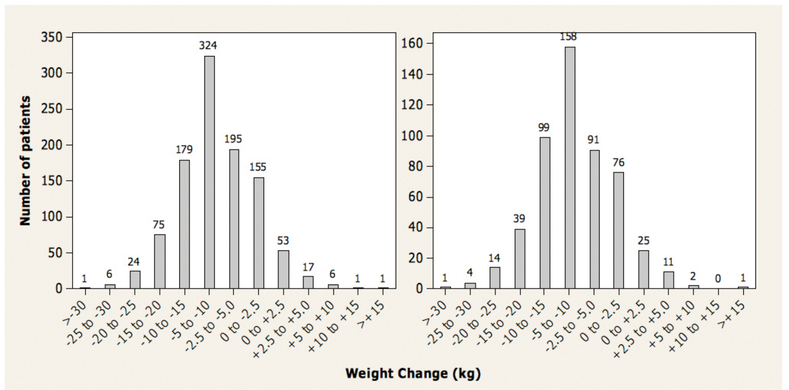


Figure 3: Range of weight changes in those who failed the NICE HbA1c criteria for success – in 1882 and 1081 patients



Proportion with any weight reduction = 92.5%

Proportion with any weight reduction = 92.5%

Figure 4: Range of %TBW changes in those who failed the NICE HbA1c criteria for success – in 1882 and 1081 patients

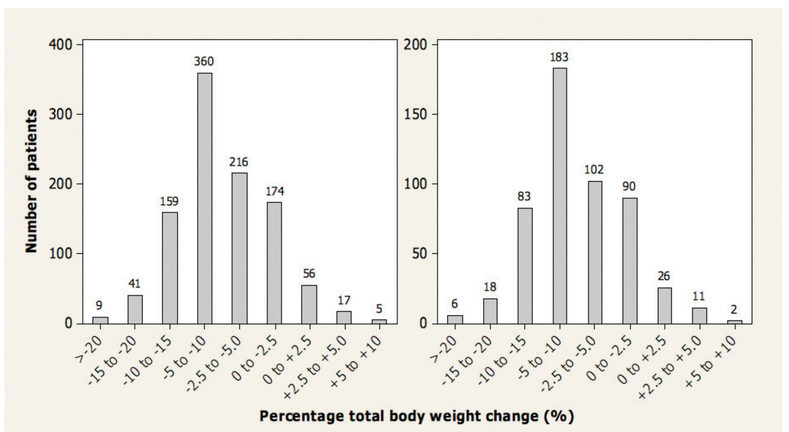
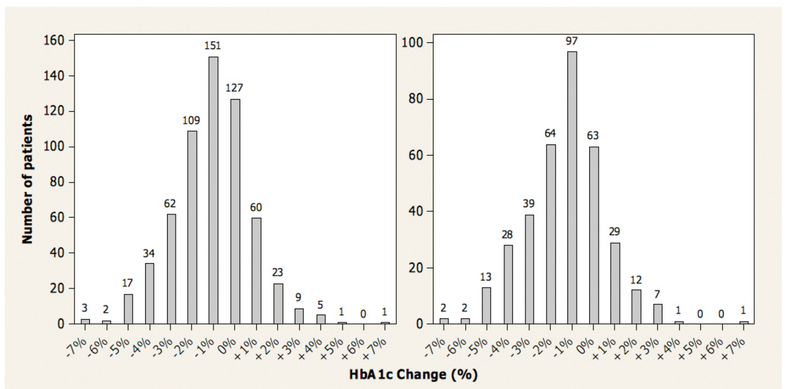


Figure 5: Range of HbA1c changes in those who failed the NICE weight criteria for success – in 1882 and 1081 patients



Proportion with any HbA1c reduction = 74.3%

Proportion with any HbA1c reduction = 77.7%

Conclusion

- Many patients would potentially have been excluded if NICE patient selection criteria were adhered to; some of these patients still responded very well to exenatide
- Selecting patients based on NICE criteria only led to marginal increase in successful treatment response
  - This was mainly driven by an improvement in HbA1c response in the context of patients who had higher baseline HbA1c, shorter duration of diabetes and not being on insulin
- Over 60% of patients achieve the ideal of both HbA1c reduction and weight loss, but only about 30% achieve the NICE guideline standard
- Many patients had a significant metabolic response but only in one parameter of HbA1c or weight
- The NICE guideline should change to acknowledge that either significant HbA1c reduction or significant weight response may represent a beneficial response

Acknowledgment

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References

1. NICE clinical guideline 87. Type 2 diabetes: the management of type 2 diabetes, **www.nice.org.uk/CG87** accessed 5 Nov 2010.

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