A RANDOMIZED ASSESSOR-BLINDED WAIT-LIST CONTROLLED TRIAL TO ASSESS THE EFFECTIVENESS AND COST-EFFECTIVENESS OF ACUPUNCTURE IN THE MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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Background

- Overall incidence of chemotherapy-related peripheral neuropathy (CIPN) is 10-35% of patients during treatment and it may be as high as 100%, depending on the chemotherapy drug, dose-intensity, cumulative dose and other as yet unidentified risk factors (Molassiotis et al 2019; Mols et al 2014; Miaskowski et al 2016).
- Significant implications of CIPN on the quality of life of patients, including dysfunction in daily activities, social well-being, work reintegration and physical impairments such as pain (Mols et al 2014).
- Considerable impact on health care resource utilization: those experiencing CIPN having more outpatient visits and medication use, estimated to be at US$17,000 more in patients with CIPN than non-CIPN cancer patients (Pike et al 2012).

CIPN management

- Largely unsuccessful
- ASCO guidelines provide no recommendation for preventing CIPN, a moderate recommendation for duloxetine in the treatment of CIPN and a few treatment options based on inconclusive evidence for CIPN (Hershman et al 2014).
- Acupuncture may be considered for treating CIPN: small scale, pilot studies (N<30) or case series provide some initial evidence of effect, particularly in decreasing neuropathic pain.
- A systematic review identified three such trials which all used a different approach (acupuncture, auricular acupuncture, acupuncture with moxibustion) (Fanconi et al 2013)

Aim of trial
(Molassiotis et al, Integr Cancer Ther, in press)

- The aim of the study is to test the effectiveness (in terms of neuropathic pain, other neurological sensations and overall quality of life) of an 8-week course of acupuncture in the management of CIPN in cancer patients who are receiving/have received neurotoxic chemotherapy.
- Assess its cost-effectiveness

Methods

- Design: randomized assessor-blinded wait-list controlled trial
- Sample size: N=87, fully-powered trial
- Settings: 2 large cancer centers in Hong Kong
- Randomization: computer-generated, balancing for treatment types
- ClinicalTrials.gov Identifier: NCT02553863

Inclusion criteria

- Patients with diagnosis of breast, gynecological, colorectal or head & neck cancer, and multiple myeloma
- Patients with cancer stage I-IV;
- Karnofsky Performance score 80-100.
- Currently receiving or having received neurotoxic chemotherapy (taxanes, cisplatin, oxaliplatin, bortezomib, etc).
- Reporting tingling in hands/feet and other clinical indications of CIPN after initiation of cancer treatments,
- Confirmed to be indicative of CIPN by a medical consultant often through brief neurological examination
- Not using any medication for the prevention or treatment of CIPN for the past 3 months.
- Willing to participate and be randomised to one of the study groups.
- No previously established peripheral neuropathy.

Intervention

- Patients received, in addition to standard care, a standardized 30-minute acupuncture session needling specific body points;
- The points were standardized according to the clinical manifestations of the subjects: For upper limbs we used LI4, LI11, PC7, TE5, and/or Baxie points (Ex-UE9)--for lower limbs we used SP6, ST36, LV3, ST41, and/ or Bafeng (Ex-LE10)
- An equal 'dose' of points was used for all patients (4 points bilaterally).
- Stimulation of the acupoints to achieve de qi sensation
- Acupuncture sessions were carried out twice weekly for 8 weeks (=a total of 16 sessions).
- Each session was based on a strict protocol followed by all therapists.

Outcome measures [*blinded assessors*]: (Baseline, week 8, follow-up wk 14 & 20)

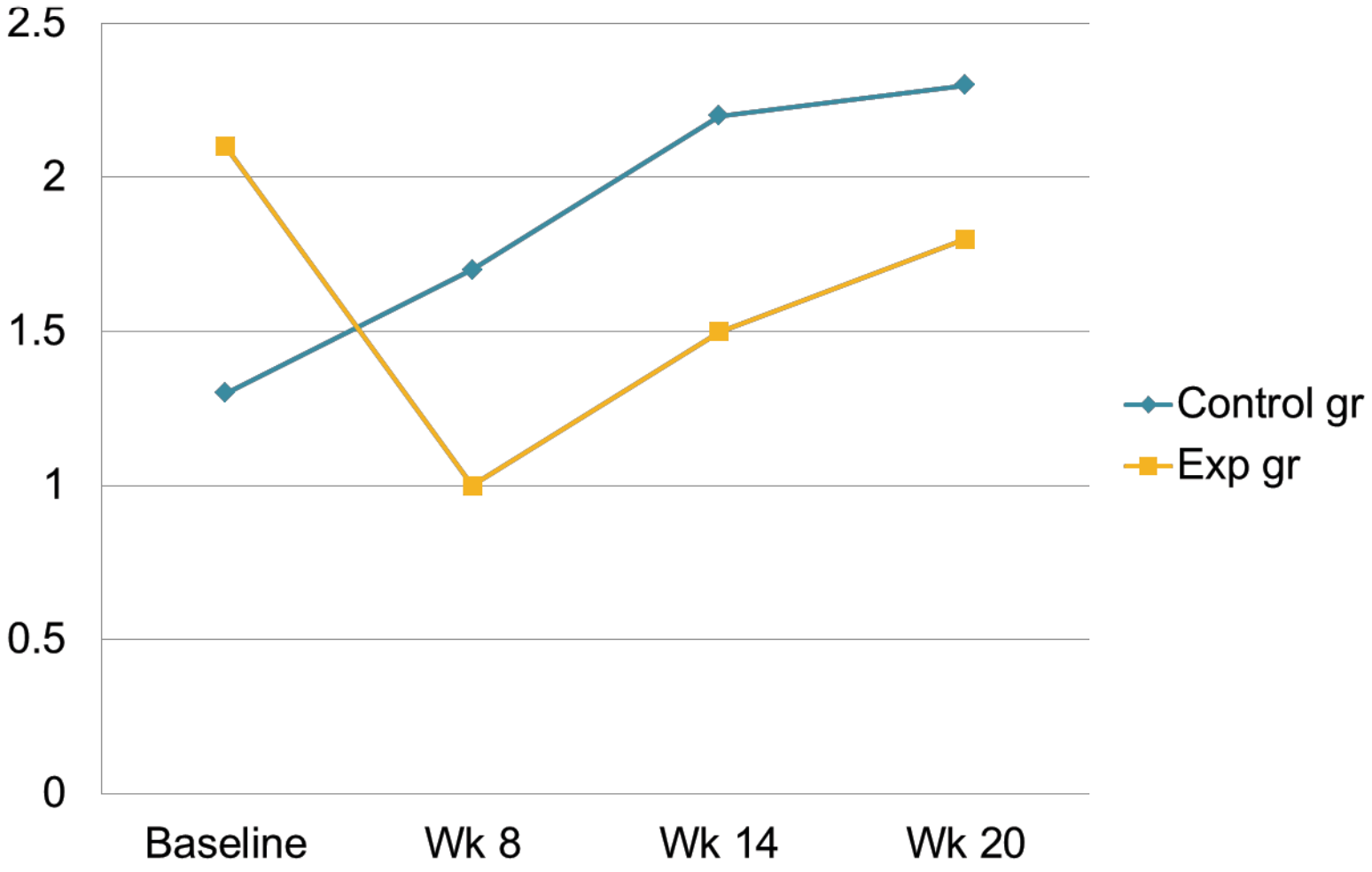
- Primary outcome at 8-weeks : Pain: '*worst pain during past week*' measured using the Brief Pain Inventory

Secondary outcomes:

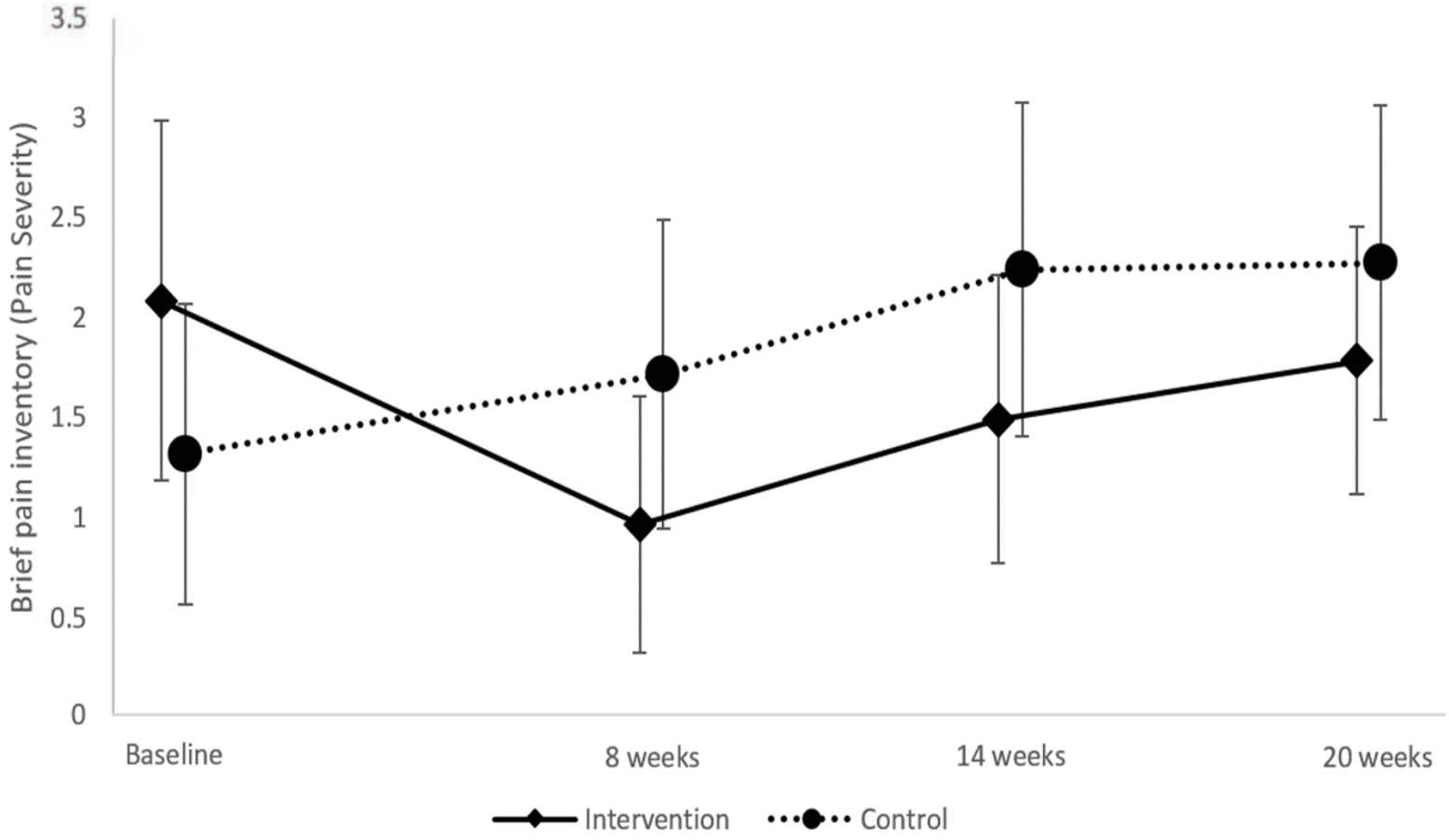
- Functional Assessment of Cancer Therapy (FACT/GOG-Ntx)
- Neurotoxicity examination [baseline and at the end of acupuncture course].
- The 7-domain Total Neuropathy Score-clinical version (TNSc).
- Neurophysiological testing (n=22)
- Health economics evaluation

Results

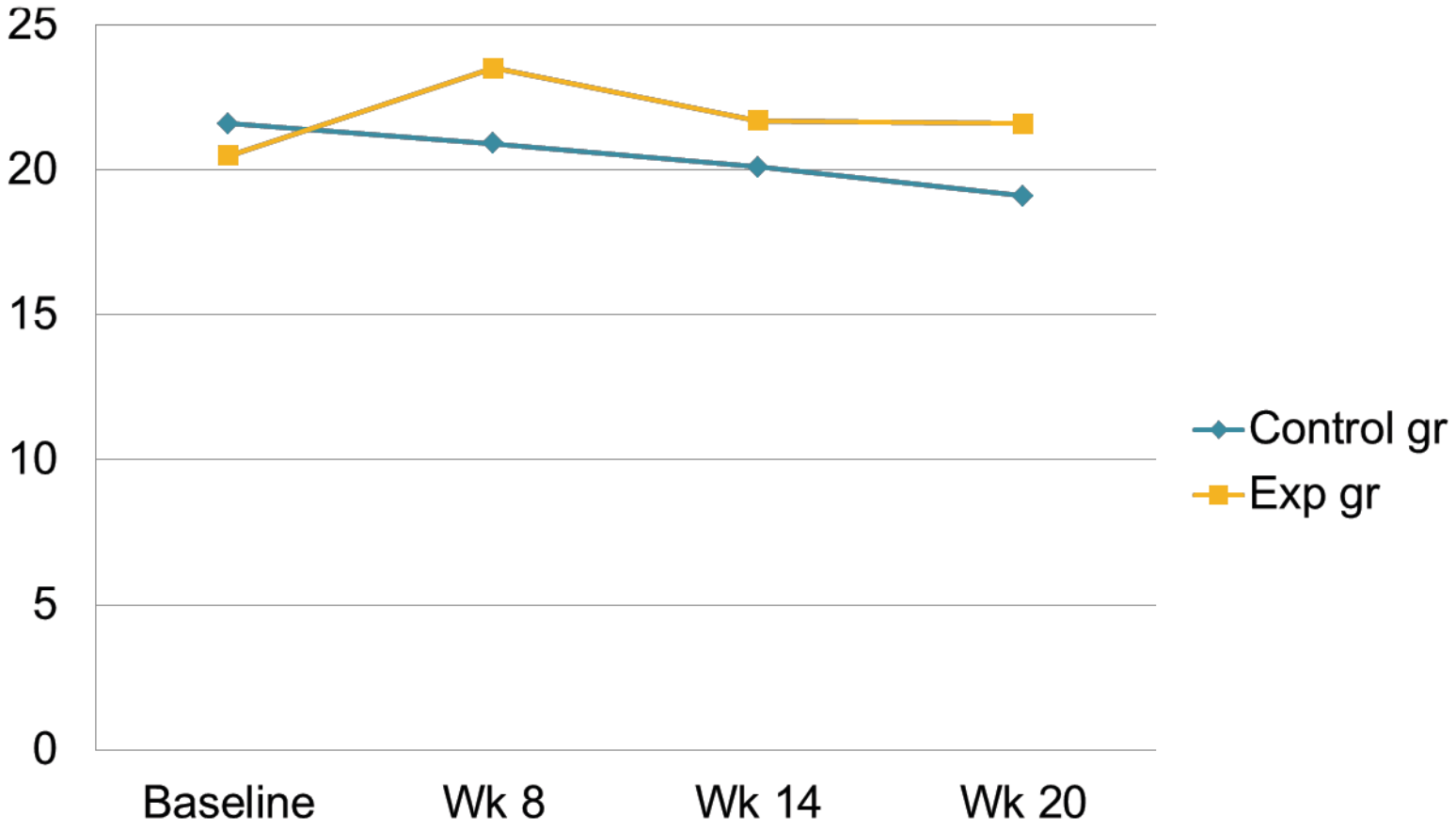
Pain severity



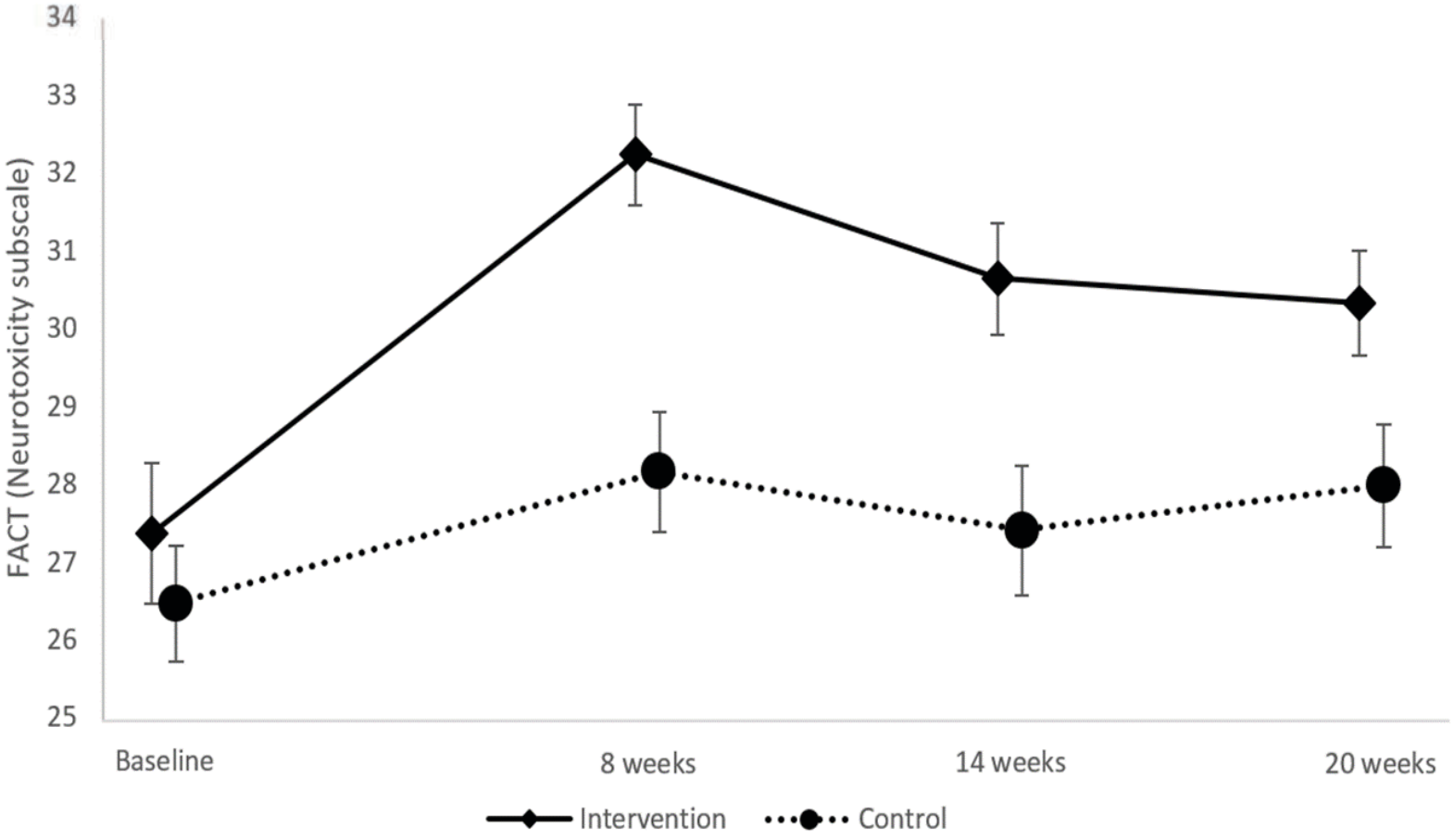
Pain intensity



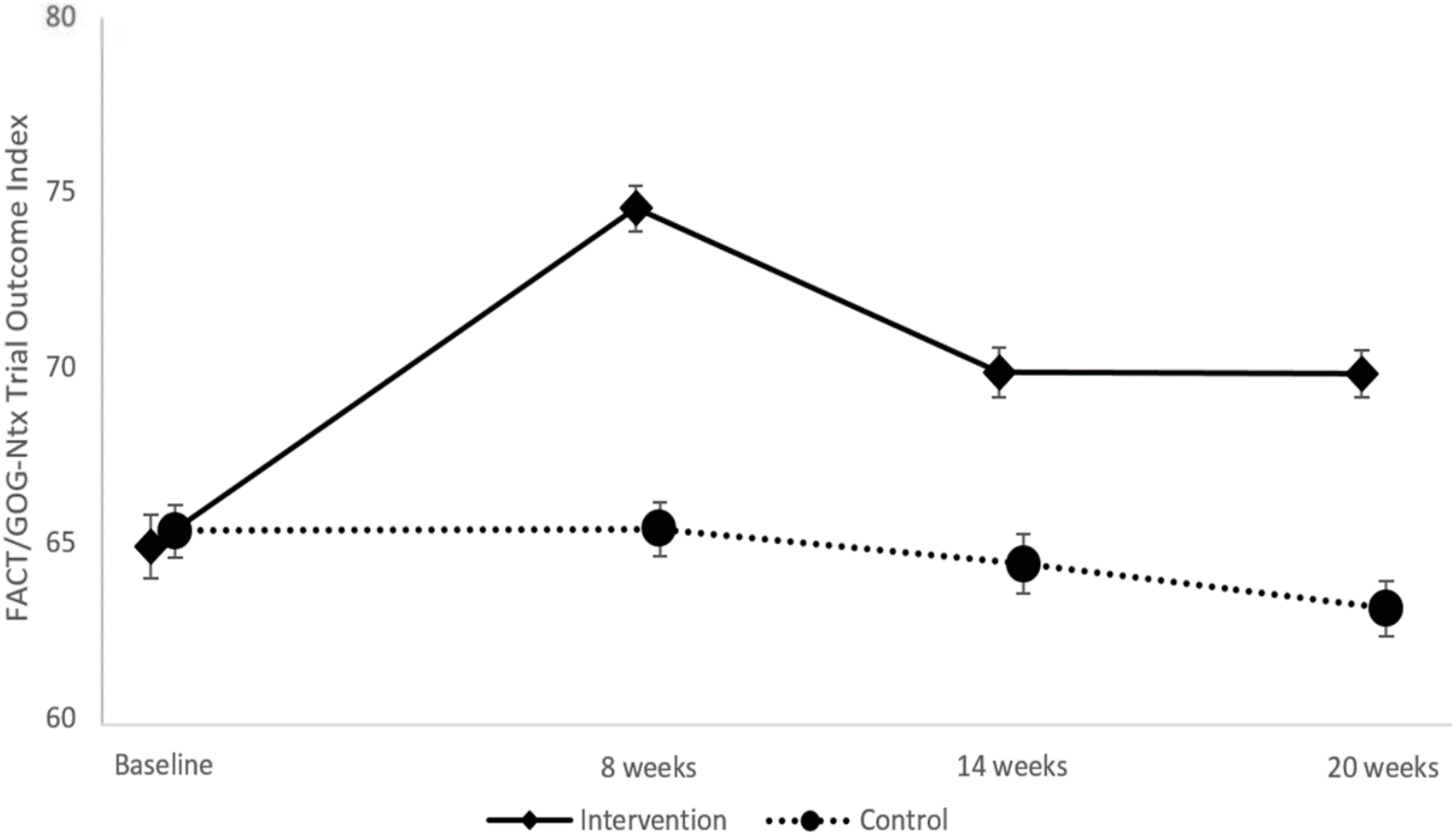
Physical well-being



Neurotoxicity score (FACT-G Ntx)



FACT/COG-Ntx Trial Outcome Index changes over time



Changes in TNS score & CTCAE

		Baseline	**8 weeks**	**p-value vs baseline**
Total Neuropathy Score (TNSc) p for group by time interaction 0.01	Control group Intervention Effect size	7.6 (0.5) 8.1 (0.5)	7.6 (0.6) 6.2 (0.5) 0.42	0.92 <0.001
p-value#		0.43	0.10	
NCI-CTCAE-sensory (Moderate/severe) p for group by time interaction 0.046	Control group Intervention	N=27 (63%) N=29 (66%)	N=26 (62%) N=16 (37%)	0.91 0.001
p-value#		0.76	0.02	
NCI-CTCAE motor (Moderate/severe) p for group by time interaction 0.07	Control group Intervention	N=30 (70%) N=33 (75%)	N=28 (67%) N=21 (50%)	0.62 0.003
p-value#		0.59	0.11	

Cost-effectiveness of acupuncture

Treatment group	Cost (HKD$) Mean (SD)	Incremental cost	QALYs Mean (SD)	Incremental QALYs	ICER (HK$/ QALY)
Health care provider perspective					
Usual care	$3,286.16 (6009.04)		0.200 (0.022)		
Acupuncture	$8,849.25 (6182.91)	$5,563.09	0.209 (0.021)	0.009	**$616,965.62**
Societal perspective					
Usual care	$12,384.40 (19230.74)		0.200 (0.022)		
Acupuncture	$19,815.03 (22955.75)	$7,430.63	0.209 (0.029)	0.009	$824,083.44
Patient perspective					
Usual care	$7,919.19 (17636.65)		0.200 (0.022)		
Acupuncture	$12,794.84 (17793.87)	$4,875.65	0.209 (0.029)	0.009	$540,727.56

Discussion

- Trial confirmed beneficial effect of acupuncture in the management of CIPN, in this first fully-powered trial
- Key outcomes met with MCID changes
- Some effects were not sustained at week 14 and 20, suggesting the need for 'boosting' sessions
- Acupuncture can be a treatment option for CIPN, in a field that options are few
- Consider 'dose', duration & acupoints
- Effective but not cost-effective treatment

?Questions and comments