

ELECTRONIC SUPPLEMENTARY MATERIAL

ESM Table 1. Summary of data extraction

Author	Country	Study design	Method(s) of neuropathy assessment used	Primary method of assessment	Pre-diabetes definition	Total sample size	Study groups (subgroups by method)	Age in years (range or mean \pm SD)	Gender (M/F)	Sample size	Participants affected, <i>n</i>	Prevalence estimate (%)
Asghar <i>et al.</i> (2014)	United Kingdom	Cross-sectional, hospital-based	Neuropathy symptom profile, McGill pain index, NCS, QST, skin biopsy, heart rate variability, deep breathing, skin biopsy and CCM	Corneal nerve fibre density ≤ 24.0 no/mm ² on CCM (using manual CCMetrics analysis)	WHO	57	IGT NGT	30-75	NR	37 20	15 NR	41 NR
Balbinot <i>et al.</i> (2012)	Brazil	Cross-sectional, hospital-based	MNSI, TRI, EMG, IDA, HRV	MNSI	ADA	79	MNSI: DM Pre-DM Control TRI: DM Pre-DM Control EMG: DM Pre-DM Control IDA: DM Pre-DM Control	55.9 \pm 9.4 56.8 \pm 12.6 45.1 \pm 14.9 55.9 \pm 9.4 56.8 \pm 12.6 45.1 \pm 14.9 55.9 \pm 9.4 56.8 \pm 12.6 45.1 \pm 14.9 55.9 \pm 9.4 56.8 \pm 12.6 45.1 \pm 14.9	9/20 3/10 16/21 9/20 3/10 16/21 9/20 3/10 16/21 9/20 3/10 16/21	29 13 37 29 13 37 29 13 37 29 13 37	2 0 0 22 10 14 16 2 0 20 10 13	7 0 0 76 77 38 55 15 0 69 77 35
Barr <i>et al.</i> (2006)	Australia	Cross-sectional, population-based	Modified NSS, modified NDS, PPS and postural systolic blood pressure drop score >20 mmHg	Neuropathy if ≥ 2 methods were abnormal	WHO	1154	IFG/IGT	≥ 25 years	NR	1084	66	6

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Bongaerts <i>et al.</i> (2013)	Germany	Cross-sectional, population-based	Interview addressing pain, presence of pain or neurological disease and history of foot ulcers or amputation; foot inspection and neurological tests of touch, vibration and temperature; ankle reflexes and sudomotor function	Vibration perception and pressure sensation	WHO	1100	<i>DM (total)</i> Known DM Newly diagnosed DM <i>Pre-DM (total)</i> i-IFG i-IGT IFG-IGT NGT	61-82	NR	239 177 62 284 55 183 46 577	49 39 10 41 3 27 11 64	21 22 16 14 6 15 24 11
Callaghan <i>et al.</i> (2016)	United States	Cross-sectional, hospital-based	Quantitative sudomotor axon reflex testing, QST, Neuro-QoL and the short-form McGill pain questionnaire	Toronto consensus definition of probable polyneuropathy	ADA	155	DM (obese) Pre-DM (obese) NGT (obese) NGT (lean)	52.9 \pm 10.2 (obese total) 48.5 \pm 9.9	48/54 (obese total) 16/37	26 31 45 53	9 9 5 2	35 29 11 4
Callaghan <i>et al.</i> (2018)	China	Cross-sectional, population-based	MNSI questionnaire, MNSI testing and monofilament testing	MNSI \geq 2.5	ADA	4002	Overall: DM Pre-DM NGT MNSI questionnaire: DM Pre-DM NGT Monofilament: DM Pre-DM NGT MNSI + monofilament: DM Pre-DM NGT	56.7 \pm 9.9 53.2 \pm 11.3 47.2 \pm 11.8	338/419 816/942 885/602 NR NR NR NR NR NR	757 1758 1487 NR NR NR NR NR NR	NR NR NR 6 2 1 9 7 4 15 6 3	
de Neeling <i>et al.</i> (1996)	Netherlands	Cross-sectional, population-based	VPT and TDT	Vibration sensation absent at big toe	WHO	597	Known DM Newly-diagnosed DM IGT NGT	65.9 \pm 6.8 65.9 \pm 6.6 65.2 \pm 6.9 63.3 \pm 7.4	30/43 42/48 78/89 134/133	73 90 167 267	50 39 27 28	69 43 16 11

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Dimova <i>et al.</i> (2017)	Bulgaria	Cross-sectional, hospital-based	Abnormal NCS and presence of symptoms or signs of neuropathy	Abnormal NCS and presence of symptoms or signs of neuropathy	WHO	478	DM IFG IGT NGT	54.4 \pm 11.5 51.7 \pm 12.1 49.2 \pm 13.5 46.6 \pm 11.4	54/67 71/54 71/31 82/48	121 125 102 130	NR	29 6 (pre-DM total) 0
Dyck <i>et al.</i> (2012)	United States	Cross-sectional, population-based	NIS and NCS	Composite scores of nerve conduction - Σ 2NC \leq 2.5th percentile	ADA	542	New DM IGT NGT	23-76 22-76 25-76	132/86 118/56 81/69	218 174 150	17 3 3	8 2 2
Franklin <i>et al.</i> (1990)	United States	Case control	History and neurological examination, QTS	2 of 3 criteria for definite neuropathy	WHO	852	DM Pre-DM NGT	20-74	NR	277 89 486	77 10 17	28 11 4
Fujimoto <i>et al.</i> (1987)	United States	Cross-sectional, population-based	NCS	NCV or distal latency $>$ 2 SD above mean in 3 nerves	WHO	229	DM IGT NGT	NR	All male	78 72 79	36 2 4	46 3 5
Fujimoto <i>et al.</i> (1991)	United States	Cross-sectional, population-based	NCS	NCV or distal latency $>$ 2 SD above mean in 3 nerves	WHO	191	DM IGT NGT	63.7 \pm 6.2 62.7 \pm 6.4 61.9 \pm 5.9	All female	52 67 72	4 1 0	8 2 0
Gabriel <i>et al.</i> (2020)	Australia, Austria, Bulgaria, Greece, Kuwait, Poland, Serbia, Spain and Turkey	Double-blind, placebo-controlled randomised controlled trial	SUDOSCAN (ESC) and MNSI questionnaire	Severe neuropathy according to electrochemical skin conductance on SUDOSCAN ($<$ 50 μ S feet or $<$ 40 μ S hands)	WHO	809	Pre-DM	45-74	339/470	809	43	5

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Herman <i>et al.</i> (1998)	Egypt	Cross-sectional, population-based	Foot examination and quantitative assessment of vibratory sensation	Vibration sensation \geq 4 SD above non-DM population aged 20-44	WHO	1451	DM Undiagnosed DM IGT NGT	>20	135/249 39/86 58/82 328/427	384 125 140 750	84 17 14 46	22 14 10 6
Kannan <i>et al.</i> (2014)	India	Cross-sectional, hospital-based	Clinical examination using NTSS and NCS	NTSS	WHO	88	IGT NGT	35-72 (total) 53.8 mean	42/16	58 30	19 NR	38 NR
Kopf <i>et al.</i> (2018)	Germany	Cross-sectional, hospital-based	NDS, NSS, NCS, short QST and long QST	Long QST	WHO	136	Long QST: DM Pre-DM Long QST + NDS: DM Pre-DM Short QST: DM Pre-DM Short QST + NDS: DM Pre-DM NDS: DM Pre-DM	64.9 \pm 2.0 60.0 \pm 3.0 64.9 \pm 2.0 60.0 \pm 3.0 64.9 \pm 2.0 60.0 \pm 3.0 64.9 \pm 2.0 60.0 \pm 3.0 64.9 \pm 2.0 60.0 \pm 3.0	67/41 13/15 67/41 13/15 67/41 13/15 67/41 13/15 67/41 13/15	108 28 108 28 108 28 108 28 108 28	103 20 103 20 53 10 81 12 68 3	95 71 95 71 49 36 75 43 63 11

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Kurusu <i>et al.</i> (2019)	Japan	Cross-sectional, population-based	Toronto consensus, ATR, QVT, sural nerve amplitude and conduction velocity on DPNCheck device	NCT on DPNCheck	WHO	625	NCT on DPNCheck:						
							Known DM	66.1 \pm 6.2	39/23	62	15	24	
							New DM	66.4 \pm 5.6	5/8	13	3	23	
							Pre-DM	65.2 \pm 7.6	57/63	120	12	10	
							NGT	60.4 \pm 9.9	159/271	430	31	7	
							Diminished ATR:						
							Known DM	66.1 \pm 6.2	39/23	62	19	31	
							New DM	66.4 \pm 5.6	5/8	13	0	0	
							Pre-DM	65.2 \pm 7.6	57/63	120	12	10	
							NGT	60.4 \pm 9.9	159/271	430	37	9	
							Abnormal QVT:						
							Known DM	66.1 \pm 6.2	39/23	62	4	7	
							New DM	66.4 \pm 5.6	5/8	13	0	0	
							Pre-DM	65.2 \pm 7.6	57/63	120	2	2	
							NGT	NR	NR	429	13	3	
							Abnormal AMP:						
							Known DM	66.1 \pm 6.2	39/23	62	9	15	
							New DM	66.4 \pm 5.6	5/8	13	2	15	
							Pre-DM	65.2 \pm 7.6	57/63	120	7	6	
							NGT	NR	NR	426	14	3	
							Abnormal CV:						
Known DM	66.1 \pm 6.2	39/23	62	9	15								
New DM	66.4 \pm 5.6	5/8	13	1	8								
Pre-DM	65.2 \pm 7.6	57/63	120	6	5								
NGT	NR	NR	429	19	5								
NCA:													
Known DM	66.1 \pm 6.2	39/23	62	15	24								
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Pre-DM	65.2 \pm 7.6	57/63	120	12	10								
NGT	NR	NR	429	31	7								

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Lee <i>et al.</i> (2015)	Canada	Cross-sectional, hospital-based	MNSI and VPT	Neuropathy defined by MNSI ≥ 2	WHO	467	DM Pre-DM NGT/NFG	53 \pm 7	126/341	22 101 344	11 50 100	50 49 29
Lin <i>et al.</i> (2012)	China	Cross-sectional, population-based	TCSS	TCSS ≥ 6	WHO	5385	DM IFG IGT IFG & IGT NGT	54.5 \pm 10.9 49.2 \pm 11.9 50.5 \pm 11.4 52.0 \pm 11.4 44 \pm 13.7	212/210 75/200 439/611 78/213 1503/1844	422 275 1050 291 3347	120 44 138 54 321	28 16 13 19 10
Liu <i>et al.</i> (2018)	China	Cross-sectional, hospital-based	NCS, SSR, CHEP and MNSI	MNSI > 2	WHO	180	Pre-DM NGT	35-81	84/96	120 60	22 NR	18 NR
Lu <i>et al.</i> (2013)	China	Cross-sectional, population-based	NDS and NSS	Symptoms and signs of neuropathy; NDS ≥ 6 with no symptoms; mild signs with moderate symptoms, NDS ≥ 3 and NSS ≥ 5	ADA	2035	DM Pre-DM NGT	64.0 \pm 9.9 61.0 \pm 9.4 59.7 \pm 11.2	230/304 357/686 141/317	534 1043 458	43 29 7	8 3 2
Németh <i>et al.</i> (2017)	Hungary	Cross-sectional, hospital-based	CPT of median and peroneal nerves using Neurometer R device	≥ 2 abnormal readings on any frequencies on the upper or lower limbs	WHO	111	IGT NGT	58.7 \pm 11.1 55.1 \pm 10.1	33/39 17/22	72 39	42 4	58 10
Oohashi <i>et al.</i> (1983)	Japan	Cross-sectional, hospital-based	ATR, PTR	† ‡	WHO	3809	DM – A DM – B IGT	> 25	2179/1630	2912 334 563	1835 157 191	63 47 34

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Saadi <i>et al.</i> (2007)	United Arab Emirates	Cross-sectional, population-based	DNES	DNES ‡	WHO	373	Diagnosed DM Undiagnosed DM Pre-DM NGT	56.0 \pm 11.6 49.9 \pm 11.8 41.4 \pm 14.3 34.6 \pm 13.7	23/34 10/30 24/61 65/126	57 40 85 191	20 6 10 NR	35 16 12 NR
Sahin <i>et al.</i> (2009)	Turkey	Cross sectional, hospital-based	MNSI and NCS	MNSI and NCS	ADA	77	MNSI: Pre-DM NGT NCS: Pre-DM	53 \pm 12 50 \pm 15 53 \pm 12	13/30 6/28 13/30	43 34 43	7 NR 9	16 NR 21
Zeng <i>et al.</i> (2018)	China	Cross-sectional, hospital-based	Dorsal-sural and medial-plantar SNAP, NCT, NDS and NSS	NCT	§	158	NCT: DM Pre-DM NGT Dorsal-sural SNAP: DM Pre-DM NGT Dorsal-sural NCV: DM Pre-DM NGT Medial-plantar SNAP: DM Pre-DM NGT Medial-plantar NCV: DM Pre-DM NGT	51.6 \pm 6.9 51.9 \pm 8.7 51.8 \pm 8.8 51.6 \pm 6.9 51.9 \pm 8.7 51.8 \pm 8.8 51.6 \pm 6.9 51.9 \pm 8.7 51.8 \pm 8.8 51.6 \pm 6.9 51.9 \pm 8.7 51.8 \pm 8.8	26/29 19/36 22/26 26/29 19/36 22/26 26/29 19/36 22/26 26/29 19/36 22/26	55 55 48 55 55 48 55 55 48 55 55 48	42 36 0 40 35 0 42 36 0 45 34 2	76 65 0 73 64 0 76 66 0 82 62 4

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Ziegler <i>et al.</i> (2008)	Germany	Cross-sectional, population-based	MNSI	Neuropathy defined by MNSI \geq 2	WHO	393	DM IFG IGT NGT	66.8 \pm 9.4 66.6 \pm 8.1 69.3 \pm 7.8 63.6 \pm 9.3	110/85 45/26 23/23 43/38	195 71 46 81	NR	28 11 13 7
Ziegler <i>et al.</i> (2009)	Germany	Cross-sectional, population-based	MNSI	Neuropathy defined by MNSI \geq 2	WHO	426	DM IFG IGT NGT	69.0 \pm 8.1 72.0 \pm 6.8 70.9 \pm 6.8 71.1 \pm 6.3	172/42 56/14 44/17 59/22	214 70 61 81	NR	39 9 25 17
Ziegler <i>et al.</i> (2012)	Germany	Cross-sectional, population-based	MNSI	Neuropathy defined by MNSI \geq 2	WHO	940	DM Pre-DM	71.8 \pm 5.5 71.5 \pm 5.2	117/84 124/107	201 231	60 45	30 20

Footnotes: **ADA:** American Diabetes Association, **ATR:** Achilles tendon reflex, **CCM:** corneal confocal microscopy, **CHEP:** contact heat pain evoked potential, **CPT:** current perception threshold, **DM:** diabetes mellitus, **DNES:** Diabetic Neuropathy Examination Score, **EMG:** electromyography, **ESC:** electrochemical skin conductance, **HRV:** heart rate variability, **IDA:** interdigital anisothermal technique, **i-IGT:** isolated impaired glucose tolerance, **IGT:** impaired glucose tolerance, **i-IFG:** isolated impaired fasting glucose, **IFG:** impaired fasting glucose, **MNSI:** Michigan Neuropathy Screening Instrument, **NCS:** nerve conduction studies, **NCT:** nerve conduction tests, **NCV:** nerve conduction velocity, **NDS:** neuropathy disability score, **NIS:** neuropathy impairment score, **Neuro-QoL:** neuropathy-specific quality of life in neurological disorders instrument, **NFG:** normal fasting glucose, **NGT:** normal glucose tolerance, **NSS:** neuropathy symptom score, **NTSS:** neuropathy total symptom score, **NR:** numerical data not reported, **OTS:** Optacon tactile stimulator, **Pre-DM:** pre-diabetes, **PPS:** pressure perception score, **PTR:** patellar tendon reflex, **QST:** quantitative sensory testing, **QTS:** quantitative tactile stimulation, **QVT:** quantitative vibration threshold, **SD:** standard deviation, **SNAP:** sensory nerve action potential, **SSR:** sympathetic skin response, **TCSS:** Toronto Clinical neuropathy Scoring System, **TDT:** thermal discrimination threshold, **TRI:** thermal recovery index, **VPT:** vibration perception threshold, **WHO:** World Health Organization. † Method of assessment not reported, ‡ definition of neuropathy not reported, § definition of prediabetes not reported.