# A systematic review and meta-analysis to quantify weight loss in pancreatic cancer: challenges using published research based on healthcare data

<sup>1</sup> School of Health Sciences, University of Surrey; <sup>2</sup> Computational Biology, Science and Technologies Facility Council; <sup>3</sup> Data Science, National Physical Laboratory

Aim To quantify the pattern (amount and timing) of pre-diagnosis weight loss in pancreatic cancer, improving its utility for early detection

## Introduction

Pancreatic cancer is relatively rare but its dismal survival rates mean that it is the sixth major cause of UK cancer mortality.<sup>1</sup> Pancreatic cancer often presents with non-specific symptoms, including weight loss. This makes early diagnosis, when curative treatment is possible, challenging. However, because weight loss occurs in most people diagnosed with pancreatic cancer, and it is often severe, it could act as a useful cancer marker.

## Methods **Open Research**

A systematic review and meta-analysis of literature was undertaken to quantify the amount and the timing of weight loss in pancreatic cancer patients. Five databases, Embase, PubMed, Scopus, Web of Science and The Cochrane Library were searched using key words including Pancreatic Cancer and Weight Loss. Additional manual searches of references were also conducted. The protocol for the review was registered on PROSPERO (CRD42022302985).



Conclusion

claire.a.price@surrey.ac.uk **@UniClairePrice** 

Claire A. Price<sup>1</sup>, Debbie Cooke<sup>1</sup>, Martyn Winn<sup>2</sup>, Nadia A. Smith<sup>3</sup>, Agnieszka Lemanska<sup>1</sup>

Method A systematic review and metaanalysis of literature to quantify weight loss patterns in pancreatic cancer

## **Methods** Studies

Observational studies containing quantitative data on pre-diagnosis weight loss were eligible for inclusion.

	Identification of studies via da	tabases and registers	Identification of s	studies via other methods
Identification	Records identified from*: Web of Science (n = 976) SCOPUS (n = 1877) PubMed (n = 861) Embase (n = 2127) Cochrane Reviews (n = 5) CENTRAL (n = 108)	Records removed <i>before</i> screening: Duplicate records removed (n = 2458)	Records identified from: PubMed Similar Articles (n = 33) Citation searching (n = 40)	
	Records screened (n = 3496)	Records excluded** (n = 3225)		
Screening	Reports sought for retrieval (n = 271) Reports assessed for eligibility (n = 262)	Reports not retrieved (n = 9)	Reports sought for retrieval (n = 73) Reports assessed for eligibility (n = 73)	Reports not retrieved (n = 0) Reports excluded: Article type (n = 16) Binary weight loss (n = 6) Treatment weight loss (n = 2) Fat proportion change (n = 2) Not specific to <u>PaCa</u> (n = 7) Weight loss not quantified (n = 27)
Included	Studies included in review (n = 27) Reports of included studies (n =13)	(n = 74)		

A total of 40 studies met this criteria, compromising 15 case-control, 7 cohort, 8 retrospective studies of medical records and 10 prospective studies of medical records. The PRISMA<sup>2,3</sup> diagram of the search is included to enable transparency and the search to be reproduced.

## **Open Research Hurdles**

- Reported measurement outcomes lack consistency in units and conventions (kg, lbs, BMI, % relative, % absolute and grouped into categories)
- Data only presented graphically or as a regression model
- Original dataset cannot be shared due to privacy
- The authors no longer have access to databases
- Reporting only selected information (e.g. only cases in case-control studies)

Studies were evaluated for bias with Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I)<sup>4</sup>. The tool includes 7 domains of bias. Two studies were excluded due to serious risk of bias Two more studies were excluded from the analysis of the case-control studies as they only reported data for cases. The results for case-control studies are shown below.

	study	Risk of bias due to confounding							Risk of bias in selection				ias in	classification of	ssification of Risk of bias due to Risk of bias due to missing data							issing data	R	isk of	bias	n mea	asurement of	Ris	Summary			
ear		1.1	1.2	1.4	1.5	1.6	overall	2.1	2.4	overall	3.1	3.2	3.3	overall	4.1	overall	5.1	5.2	5.3	5.4	5.5	overall	6.1	6.2	6.3	6.4	overall	7.1	7.2	7.3	overall	risk of bia
ase Control																																
)12	Ben et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	Ν	MODERATE	Ν	PY	PN	SERIOUS	Ν	LOW	N	Y	Ν	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Υ	Y	MODERATE	SERIOUS
	Talar-Wojnarowska																															
120	et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	N	MODERATE	Y	Y	PN	MODERATE	N	LOW	N	Y	N	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
21	Brewer et al	PN	-	-	-	Ν	LOW	Ν	N	LOW	Y	Y	PN	LOW	Ν	LOW	Y	Ν	N	NI	NI	MODERATE	PN	PN	Y	PN	LOW	Y	Y	Y	MODERATE	MODERAT
)12	Lee et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	Ν	MODERATE	Y	Y	PN	MODERATE	Ν	LOW	Y	Ν	N	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
08	Chari et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Υ	PN	LOW	Ν	LOW	N	Y	Υ	NI	NI	MODERATE	PN	Υ	Y	PN	MODERATE	Y	Ν	Ν	MODERATE	MODERAT
19	Sah et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Y	PN	LOW	Ν	LOW	Y	Y	Y	NI	NI	MODERATE	PN	Υ	Υ	PN	MODERATE	Y	Υ	Υ	MODERATE	MODERAT
08	Pannala et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Υ	PN	LOW	Ν	LOW	Y	Y	Y	NI	NI	MODERATE	PN	Y	Ν	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
13	Mizuno et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	Ν	MODERATE	Y	Y	PN	LOW	Ν	LOW	Y	Y	Y	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
09	Pannala et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Y	PN	LOW	Ν	LOW	N	Y	Y	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Ν	Y	Y	MODERATE	MODERAT
18	Mueller et al	PN	-	-	-	Ν	LOW	Ν	N	LOW	Y	Y	PN	LOW	Ν	LOW	Y	Y	Y	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
21	Khan et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	Ν	LOW	Y	Y	PN	LOW	Ν	LOW	N	Y	Y	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Ν	Ν	Ν	LOW	MODERAT
19	Mueller et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Υ	PN	LOW	Ν	LOW	Y	Y	Υ	NI	NI	MODERATE	PN	Υ	Y	PN	MODERATE	Y	Υ	Y	MODERATE	MODERAT
21	Hue et al	PN	-	-	-	Ν	LOW	Ν	Ν	LOW	Y	Υ	PN	LOW	Ν	LOW	N	Y	Υ	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
11	Hart et al	PY	Ν	PY	PY	Ν	MODERATE	Ν	Ν	LOW	Y	Y	PN	LOW	Ν	LOW	N	Y	Y	NI	NI	MODERATE	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT
16	Olson et al	PN	-	-	-	Ν	MODERATE	Ν	Ν	LOW	Y	Y	PN	LOW	Ν	LOW	Y	Y	Y	Y	Y	LOW	PN	Y	Y	PN	MODERATE	Y	Y	Y	MODERATE	MODERAT

## Discussion

Examining weight loss prior to pancreatic cancer diagnosis is complicated by the weight loss seen in the majority of cancer patients (cancer cachexia).

Another complication is the diabetes status of pancreatic cancer patients as approximately 40-65% will develop new-onset diabetes.<sup>5</sup> However, it appears that weight loss patterns become distinct over the year prior to pancreatic cancer diagnosis.<sup>6</sup>

Study populations often lack ethnic diversity.

### Detecting weight loss early is vital to improve diagnosis of pancreatic cancer to improve survival rates

Weight measurements should be more frequent than annual check-ups

### Weight loss data should be reported in a standard format (kg and a percentage of weight lost) in literature to allow comparison of studies

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**Challenges:** Healthcare data is usually closed making analysis harder **Successes: PROSPERO** registration

## **Study Quality**

## Results Weight Loss Amount

Case-control studies show that 45-75% of pancreatic cancer patient lose ≥3% of their body weight<sup>6–10</sup> with 16-21% losing  $\geq$ 15%.<sup>7,9,10</sup> Greater weight loss is linked with poorer prognosis.

## Results Weight Loss Timing

Weight loss can begin to be detected up to two years before pancreatic cancer diagnosis,<sup>11,12</sup> with greater divergence between cases and control seen 1 year prior to diagnosis.<sup>6,8,11–14</sup> Most of the weight loss occurs in the six months prior to pancreatic cancer diagnosis.<sup>8,14</sup>

This weight loss occurs as part of a suite of metabolic changes<sup>6,12</sup> which appear to be distinct from cachexia and other cancer symptoms.<sup>6,11,13</sup> It is likely that the maximum possible time this approach will accelerate the detection of pancreatic cancer is six months.

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## **Open Research**



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