**Reference article and other IMP info.**

**No.8->**

**{ The aim** of this study was to report survival by intention to treat in a comparison of upfront surgery versus neoadjuvant treatment in resect-able or borderline resect-able pancreatic cancer.

**Results:** In total, 38 studies were included with 3484 patients, of whom 1738 (49·9 per cent) had neoadjuvant treatment. The weighted median overall survival by intention to treat was 18·8 months for neoadjuvant treatment and 14·8 months for upfront surgery; the difference was larger among patients whose tumours were resected (26·1 *versus* 15·0 months respectively). The overall resection rate was lower with neoadjuvant treatment than with upfront surgery (66·0 *versus* 81·3 per cent; *P* < 0·001), but the R0 rate was higher (86·8 (95 per cent c.i. 84·6 to 88·7) *versus* 66·9 (64·2 to 69·6) per cent; *P* < 0·001). Reported by intention to treat, the R0 rates were 58·0 and 54·9 per cent respectively (*P* = 0·088). The pathological lymph node rate was 43·8 per cent after neoadjuvant therapy and 64·8 per cent in the upfront surgery group (*P* < 0·001). Toxicity of at least grade III was reported in up to 64 per cent of the patients.

**Conclusion:** Neoadjuvant treatment appears to improve overall survival by intention to treat, despite lower overall resection rates for resectable or borderline resectable pancreatic cancer.

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**1.R0 resection** indicates a microscopically margin-negative **resection**, in which no gross or microscopic tumor remains in the primary tumor bed.

**2.R1 resection** indicates the removal of all macroscopic disease, but microscopic margins are positive for tumor.

**3.Quality-adjusted life year:**

The QALY is a measure of the value of health outcomes to the people who experience them. It combines two different benefits of treatment - length of life and quality of life - into a single number that can be compared across different types of treatments.

Calculating a QALY requires two inputs. One is the [utility](https://en.wikipedia.org/wiki/Utility) value (or utility weight) associated with a given state of health by the years lived in that state. The underlying measure of utility is derived from clinical trials and studies that measure how people feel in these specific states of health. The way they feel in a state of perfect health equates to a value of 1 (or 100%). Death is assigned a utility of 0 (or 0%), and in some circumstances it is possible to accrue negative QALYs to reflect health states deemed "worse than dead."[[3]](https://en.wikipedia.org/wiki/Quality-adjusted_life_year#cite_note-Weinstein2009-3) The value people perceive in less than perfect states of health are expressed as a percent between 0 and 1.

The second input is the amount of time people live in various states of health. This information usually comes from clinical trials.

To calculate the QALY, the two measures are multiplied. For example, one year lived in perfect health equates to 1 QALY. This can be interpreted as a person getting 100% of the value for that year. A year lived in a less than perfect state of health can also be expressed as the amount of value accrued to the person living it. For example, 1 year of life lived in a situation with utility 0.5 yields .5 QALYs - a person experiencing this state is getting only 50% of the possible value of that year. In other words, they value the experience of being in less than perfect health for a full year as much as they value living for half a year in perfect health (0.5 years × 1 Utility). This characteristic is what makes the QALY useful for evaluating tradeoffs.

**No.9->**

**{Objective:** Controversy remains existed whether chemoradiotherapy (CRT), especially neoadjuvant chemoradiotherapy (neoadjuvant CRT) achieves a significant benefit in resectable pancreatic cancer (PC) treatment. In this meta-analysis, we aimed to clarify the benefits of CRT and neoadjuvant CRT in resectable PC

**Conclusions:** This meta-analysis showed that CRT showed no significant effect on OS and PFS when compared to non-CRT. Neoadjuvant CRT showed no significant effect over postoperative adjuvant CRT.

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**4.Exploratory laparoscopy**

It is also termed diagnostic laparoscopy, is a minimally invasive method for the diagnosis of intra-abdominal diseases through direct inspection of intra-abdominal organs. Exploratory laparoscopy also allows tissue biopsy, culture acquisition, and a variety of therapeutic interventions

**5.Postoperative complications**

They are problems that can happen after you have had surgery but which were not intended. Doctors are aware of the risk of complications and take steps before, during and after surgery to reduce this risk. However, some complications are common and occur frequently despite precautions.

**6.Retrospective study**

A study that compares two groups of people: those with the disease or condition under study (cases) and a very similar group of people who do not have the disease or condition (controls).

**7.Prospective Study**

A prospective study watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort of subjects and watching them over a long period. The outcome of interest should be common; otherwise, the number of outcomes observed will be too small to be statistically meaningful.

**No.24->**

**{Statistical Analysis:**

Pooled estimates of proportions with corresponding 95% confidence intervals were calculated on the base of the Freeman-Tukey double arcsine transformation [[30]](https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000267#pmed.1000267-Freeman1),[[31]](https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000267#pmed.1000267-Miller1) within a random effect model framework.

preliminary simulation studies suggest that unbiased pooled estimates of median survival times cannot be achieved by simple weighted averaging of medians. A more appropriate approach is achieved by averaging parameter estimates of a presumed density function of survival and recalculating the estimate of median from the pooled distribution parameter. A reasonable distribution of survival times which implies a time constant hazard rate corresponding to the sole distribution parameter λ is given by the exponential distribution. Following this assumption, a weighted estimate of population median (mp) survival is derived by:



->where **mi** denotes the median survival within a study population i (with i from 1 to k)

-> **wi** refers a study specific weight function, and Σwi = 1.

Since no sufficient information on patients at risk for median survival times was available from the considered studies, number of study participants (divided by the total number of evaluable patients) was used as weights.

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