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Health Economic Calculations on Low-Dose Aspirin and as an Additional Cancer Therapy

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Abstract

There is highly suggestive evidence that low-dose aspirin (LDA), 75-150 mg per day, could help improve adult cancer survival by 20%. The Quality Adjusted Life Year (QALY) is a combined metric of length of life and quality of life. A cost estimate of £10 per annum per patient for LDA was taken for a health economic model of a cohort of 100 adult cancer patients. The overall years gained based on this calculation is that 10 extra patients will live an extra 10 years for every 100 adult cancer patients taking LDA. If these 10% of patients equally share a 100% boost to their quality of life, then each patient will also receive a 10% boost to the quality of life per annum. Based upon a 10% boost to the quality of life, an estimate of £100 per QALY from LDA was made, which would make this option highly cost-effective as compared to standard health economic metrics that is used by medical regulators. From a health economic perspective, LDA should be seriously considered an additional treatment in adult cancer patients.

Keywords: Aspirin, Cancer, Health Economics, QALY

1. Introduction

Cancer survival is highly dependent on the stage of diagnosis and the organ affected [1]. For example, over 5 years testicular cancer has a survival rate of over 90% while pancreatic cancer has a survival rate of under 10% [1]. Clearly, the treatment agreed with the patient will also impact on their quantity of life and there is sometimes a trade-off between length of life and quality of life [2]. The National Health Service (NHS) of the United Kingdom is a publicly funded healthcare organisation and one of the medical regulators of the NHS is the National Institute for Health and Social Care Excellence (NICE). To inform decision making, one of the tools used by NICE is the Quality Adjusted Life Year (QALY) [3]. The QALY is a combined metric of length of life and quality of life. Another factor important in respect of medical regulation is cost. NICE consider an intervention costing the NHS under £20,000 per QALY gained as cost effective [4]. In the case of cancer treatment, there is highly suggestive evidence from observational studies that low-dose aspirin (LDA), 75-150 mg per day, could help improve cancer survival, in most if not all types of the disease, by 20% [5]. The observational studies are supported strongly by plausible mechanisms of action.

Aspirin is an inexpensive and easily available medicine that is already widely used for the treatment of vascular disease although at present, the use of the medicine in treating cancer is limited. LDA is used in the treatment of some blood cancers and randomised trials are ongoing with the medicine in some of the more common types of solid cancer, such as bowel and breast [6,7]. Some cancer patients will also have co-morbid vascular disease and it has been estimated that about 25% of adult cancer patients are already taking LDA [8]. This paper sets out to provide health economic estimates of LDA as an additional cancer treatment in adult patients based on modelling of benefits and costs.

2. Methods

Data on average adult cancer survival for 1,5 and 10 years was sourced from Cancer Research UK [9]. It was assumed that LDA would boost this by 20% albeit a key planning assumption was also made. LDA, like all medicines, is associated with risks and it was assumed that adult cancer patients with contraindications to the medicine would be identified and advised not to take it as part of good medical care. For this reason, no estimates were made about the potential harms caused by LDA, such as internal bleeding occurring in the stomach [10]. The estimated additional survival from LDA in terms of length of life was calculated by increasing current survival rates by 20%. This assumes that across the ten-year survival interval, 1 in 5 more adult cancer patients would be alive if they took LDA compared to adult cancer patients not taking the medicine. Using these measures, the extra survival after 10 years from LDA can be calculated using the 2 equations below, both of which are equivalent in their outcomes.

Equation 1: 10-year survival boosted by LDA = Current ten-year survival * 1.2
Or Equation two = Current ten-year survival + Current ten-year survival * 0.2

Based on this estimated increased survival due to taking LDA, a total number of extra years was calculated based on a cohort of 100 patients with current average adult cancer survival. Based on these extra years of survival, the increase each adult cancer patient might gain was estimated by using the following equation which assumed an equal distribution of quantity of life:

ISPP = (CTYS * IBA) / CN where each aspect is defined as
ISPP = Increased survival per patient (average)
CTYS = Current ten-year survival
IBA = Increased by LDA (20%)
CN = Cohort number of 100 patients

The quality-of-life gain was estimated by dividing the overall increased survival per patient across the cohort of 100 by the additional number of patients alive after 10 years from LDA use. The assumption underpinning this calculation was that on a scale 0 to 1, where 0 is dead and 1 is perfect health, cancer patients would fall somewhere within this range. So, to illustrate this, a 0.5 increase in quality of life would equate to a 50% boost in quality of life It was further assumed that the patients who lived the longest taking LDA, in this case 10 years, would equally share the quality-of-life gain given their additional survival length. As for the costs of LDA, there was no agreed figure to use. LDA is widely and easily available in the United Kingdom as an over-the-counter medicine. It can be purchased in pharmacies, supermarkets and via online delivery sites. Reviewing some of the largest suppliers of LDA, most of these had a cost of 30 tablets of LDA, a month's supply, at less that £1. Given the lack of an agreed figure, an estimate of £10 per annum for LDA was therefore taken. This assumes that an individual adult cancer patient has decided to purchase their own LDA after first discussing their treatment with a member of their healthcare team. The only final calculation to perform was the cost per QALY from LDA. This was calculated by the following equation which combined both the cost element of LDA along with the calculated boosted quality of life in adult cancer patients.

QALY of LDA = Cost of LDA / Boosted quality of life from LDA

3. Results

Cancer Research UK data on 1,5- and 10-year overall survival rate for adults with cancer is about 70%, 55% and 50% respectively. Using the estimate of a 10-year survival currently of 50% being boosted by a further 20% with LDA, then for adult cancer patients taking LDA a further 10 would be alive after ten years. This is calculated as either (50/100*1.2) or (50/100 + 50/100*20/100) = 60% or 60 per 100 adult cancer patients taking LDA. Figure 1 below shows this pictorially.

LDA 10% net survival boost = 60 per 100 with LDA minus 50 per 100 without LDA

Figure 1: Comparing Adult Cancer Survival After 10 Years with and Without LDA

It can therefore be calculated that if 100 adults with cancer take LDA, after 10 years an additional 10 further patients could survive. This is calculated as 50% survival after 10 years boosted by 20% or an additional 1 in 5 patients alive after 10 years. If 50 patients per 100 are alive as per 50%, then 10 patients more may survive if they take LDA, meaning 60 patients or 60% survival after 10 years. The overall years gained based on this calculation is that 10 extra patients will live an extra 10 years for every 100 cancer patients taking LDA. This is calculated as extra cancer patients alive * extra 10 years gain or for the cohort of 100 adults cancer patients, calculated as 10*10. This gives 100 extra life years for every 100 cancer patients taking LDA so an average extra survival may be calculated. This equates to an additional average of 1 extra life year per patient, calculated as extra life years / cohort size or specifically 100 years extra /100 patients. This of course will range from those who might receive little benefit to those who receive a large and longer-term benefit, including boosting surviving to 10 years. It can be further assumed that each patient has the opportunity to purchase the LDA over-the-counter albeit after first discussing this with their healthcare team. This can be estimated as a cost of £10 per year as 30 tablets, or a month supply, costs less than £1 in many pharmacies, a cost of £10 per life year gained. It can be further assumed that any side effects from LDA would be minimal. Cancer patients will be under the care of

a healthcare team so could be carefully monitored and any contraindications to LDA identified prior to starting it.

It could be argued that there would be an additional cost of discussing LDA in a consultation between a healthcare professional and a cancer patient. At most, this would be a highly marginal cost and 1 in 4 cancer patients might already be taking LDA for vascular disease protection, so it is unlikely to incur major cost. Another assumption is that the 10 additional patients per 100 who survive 10 years will experience an improvement in their quality of life. Whilst this might be true for all cancer patients who take LDA, those patients who respond well to the medicine could gain improvements as measured by Quality Adjusted Life Years (QALY's). If the 10 patients per 100 who have the best response by having the longest survival each share a full QALY per annum, then each one will receive a 10% boost to their quality of life. This is calculated by 10 patients each sharing a full QALY, therefore 1 full QALY / 10 = 0.1 or 10%. So, the QALY gained from LDA would be the cost of a year of treatment discounted by the boost to quality of life. Or £10 divided by 10%, giving a QALY estimate of £100 per annum. This is mainly due to the low-costs of LDA and supplementary files give further data.

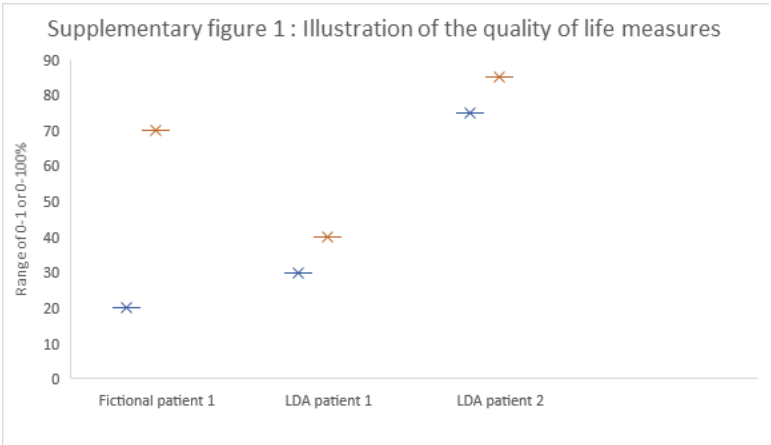
4. Discussion

This paper has offered a desktop calculation of health economics for LDA as an additional treatment in adult cancer patients. One of the main limitations to this is the lack of direct empirical evidence about the quality of life gain adult cancer patients might gain from taking LDA. Such data might be available in due course from randomised controlled trials although even at a small gain of 10%, LDA is still highly cost effective at £100 per QALY per patient per annum when compared against a medical regulator who sets the threshold at £20,000.

Another limitation to this study is the lack of sensitivity analysis, both in respect of modelling different costs of LDA and different estimates on survival. Within the current analysis, LDA estimated QALY at £100 is 200 times more cost-effective than that of a medical regulator and therefore given the inexpensive nature of aspirin, a 200-fold less impact on quality of life would still be effective. Based on a 0.1 or 10% improvement in quality of life, which itself seems modest, even a 200-fold reduction in this estimate would still be cost effective. That means that if every adult cancer patient who took LDA experienced a (10/100)/200 or 0.0005 or 0.05% improvement to their quality of life, then LDA would still be cost-effective. So even a very small improvement to quality of life would be beneficial given how inexpensive LDA is and given it is easily sourced.

In conclusion, from a health economic perspective, LDA should be seriously considered an additional treatment in adult cancer patients. The main safeguards on this are that adult cancer patients should only start to take LDA after consultation with their healthcare team. Self-medication on any medicine has risks and the other disadvantage if patients do self-medicate, where LDA would not be on the medical records, is that it prevents the use of routine data to explore the relationship between LDA, quality of life and quantity of life.

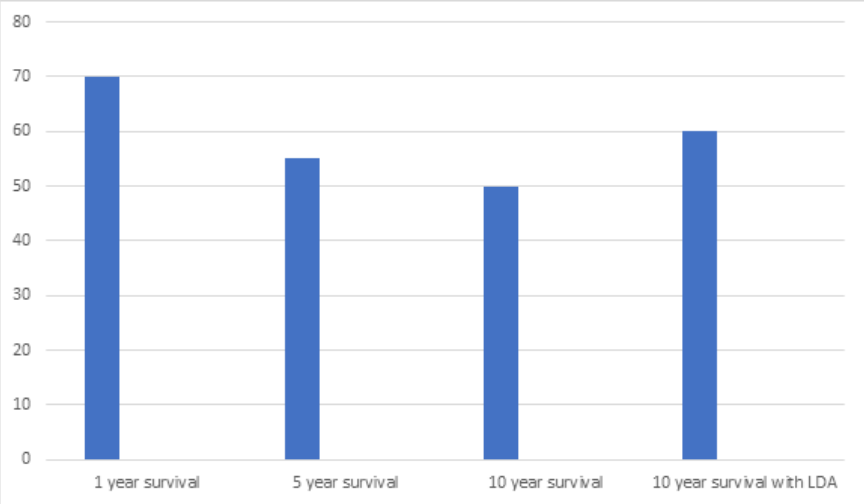
Supplementary Files



Supplementary Figure 1: Illustration of the Quality of Line Measures

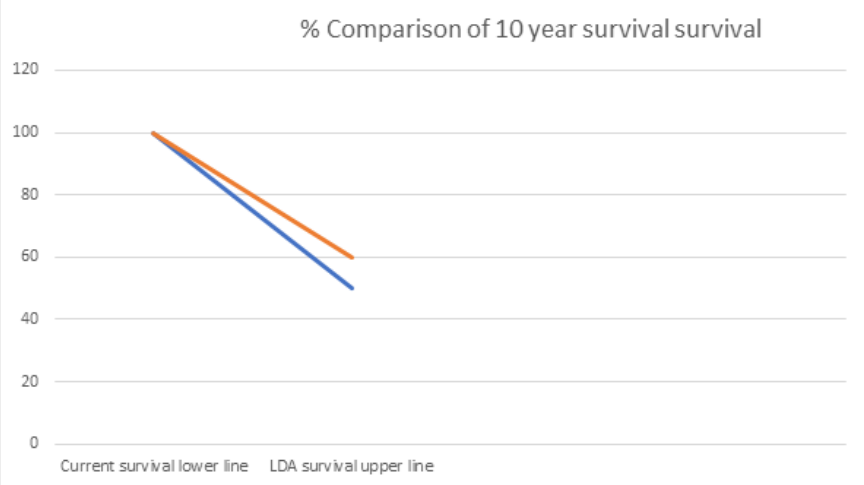
The above describes three scenarios to illustrate quality of life gain. Blue represents pre-intervention and orange represent post-intervention. Fictional patient 1 is a non-cancer patient, just to illustrate the principle. They have chronic pain which limits their daily functioning and report poor quality of life, subjectively graded at 20% or 0.2. They are given a new analgesic medicine which proves transformative and allows them to fulfil a lot of their ambitions. They subjectively report to their healthcare team how life has improved to 70% or 0.7, giving a quality-of-life gain of 50% or 0.5. LDA patient 1 is an adult cancer patient with a lot of co-morbidity, including compromised mental health. They report a low quality of life of 30% or 0.3, feeling only one third fulfilled in their life compared to prior to their cancer diagnosis. They start taking LDA after a discussion with their healthcare team and the potential for them to live longer and spend more time with their family gives them a quality-of-life boost of 10% or 0.1 to 40% or 0.4. LDA patient 2 has cancer and

has remained positive since their diagnosis, seeing each day as an opportunity to embrace life. They report a 75% or 0.75 quality of life, slightly lower than prior to their diagnosis on the pragmatic basis that life is never perfect so 100% is unachievable. They start taking LDA after a discussion with their healthcare team and feel psychologically boosted by an extra 10% or 0.1 by the possibility that their life might be extended. Whilst taking LDA, they subjectively report that life is as good as possible, grading it at 85% or 0.85. A number needed to treat (NNT) figure can also be calculated from these estimates for LDA to produce 1 extra adult cancer patient alive after 10 years as 10, that is the number of extra cancer patients alive after 10 years divided by the cohort size, or 10 / 100 or a ratio of 1 to 10. This means that in clinic list of X adult cancer patients, then X/10 could be estimated to have 10-year survival from LDA. That is not to say other patients will have no benefit but merely to provide a summary statistic of NNT.



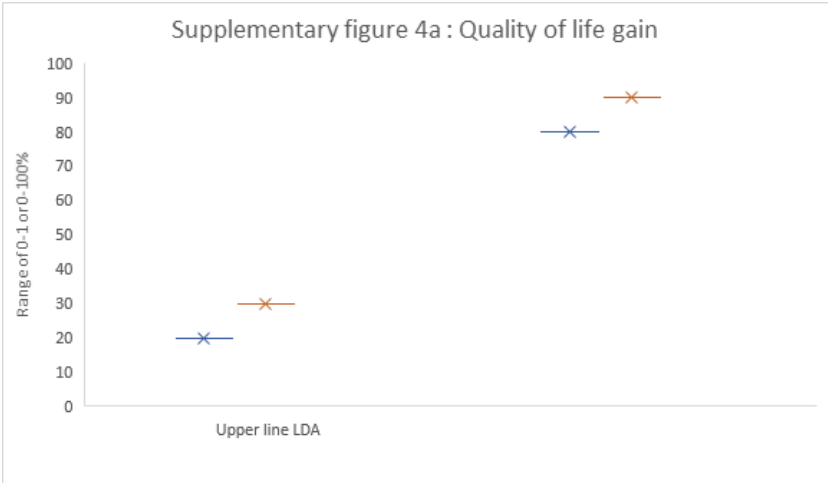
Supplementary Figure 2: UK Current Cancer % Survival and Possible 10 Year % Survival with LDA

This figure highlights the possibility that more adult cancer patients taking LDA survive 10 years than non-LDA adult cancer patients survive after 5 years. Clearly this is only a model that needs to confirmed or refuted by more research.

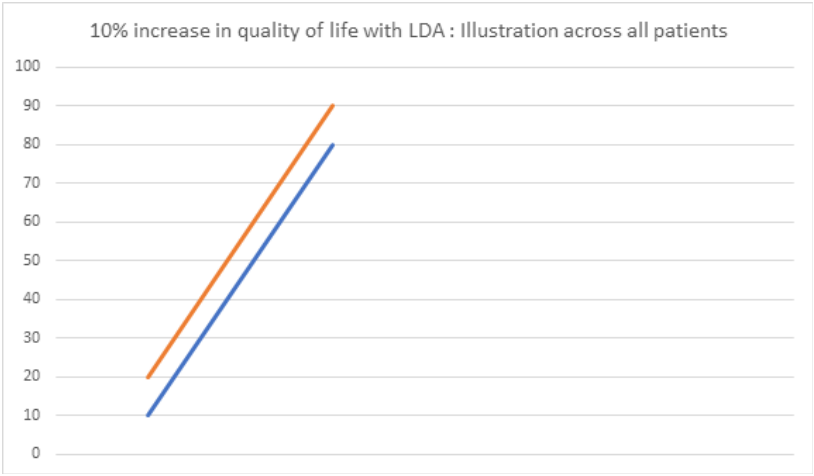


Supplementary Figure 3: Survival Comparison with LDA and no LDA

The aboive is a crude illustration based on 10 year survival rates, showing a 10% advantage.

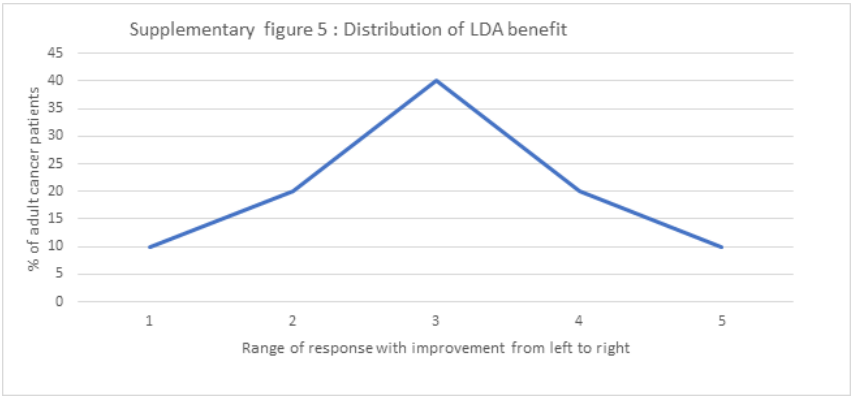


Supplementary Figure 4a: Quality of Life Gain



Supplementary Figure 4b: Boost to Quality of Life Across Adult Cancer Patients

Supplementary figures 4a and 4b respectively show point estimate and a linear line. The assumptions to this are that for patients with a very low quality of life of 10%, LDA could still offer a valid QALY gain and this is true for those with a high quality of life of 80%. Future research could undertake a sensitivity analysis of a quality-of-life gain of 5% plus or minus 5% with LDA to acknowledge a range of effects. Based on previous calculations, even if there was a 5% quality of life gain, the QALY gain would be £200 per annum which is still hugely cost effective.



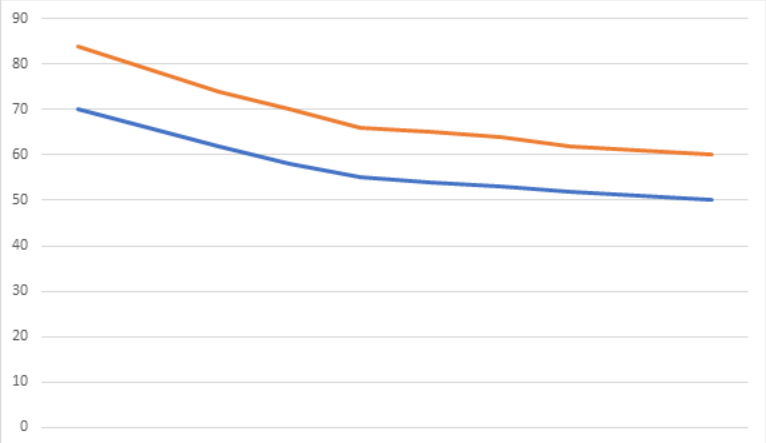
Supplementary Figure 5: Distribution of LDA Benefit

The above models a potential distribution of patient response to LDA. Assuming that 10% have a very good response, it seems reasonable to assume a symmetrical distribution where 10% will have a small response to LDA. The above suggests that most adult cancer patients would have at least some degree of positive response to taking LDA and again, further work on this is needed.

100 Patients	Patients alive	LDA patients alive	Net patients
Year 1	70	84 (70 * 1.2)	14
Year 2	66	79	13
Year 3	62	74	12
Year 4	58	70	12
Year 5	55	66	11
Year 6	54	65	11
Year 7	53	64	11
Year 8	52	62	10
Year 9	51	61	11
Year 10	50	60	10
Extra survival			115

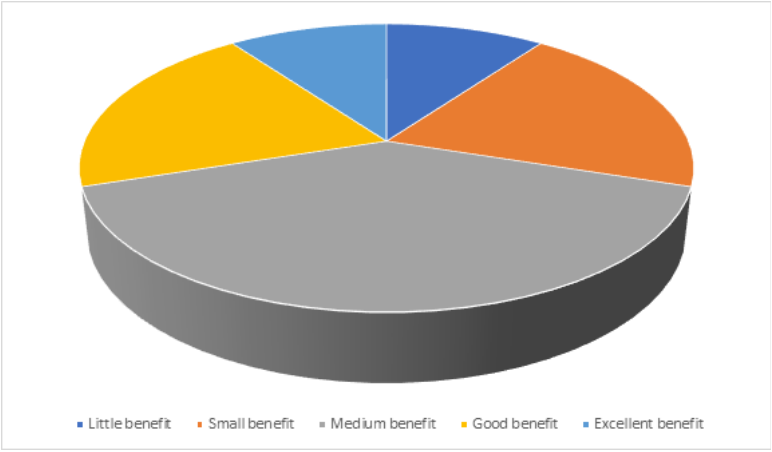
Supplementary Table 1: An Arithmetic Estimation to Extended Survival

Based on an arithmetic estimation, there would be 115 patients surviving one extra year for every 100, slightly higher than the multiplied version in the main paper. This is still approximately equivalent to an average one-year life gain per patient. The patients alive use 1,5- and 10-year survival and estimates made that that the survival reduced in similar integers between these known values.



Supplementary Figure 6: Possible 10 Year Improved Survival from Low-Dose Aspirin

The above is based on supplementary table 1 and provides a more nuanced estimate of the adult cancer survival from low dose aspirin, which is shown as the top line versus current survival as the lower line. The intermediate data from the known 1-, 5- and 10-year survival assumes that the fall in survival rate is similar and therefore the two lines are almost parallel across the full 10-year interval.



Supplementary Figure 7 : Distribution of Benefit from Low-Dose Aspirin

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