Executive summary

**The outcome of Liver Intervention OR Surveillance in DiSappearing colorectal liver Metastases (LORDS-M Study)**

Follow this link for further information and registration

(<https://www.abdn.ac.uk/iahs/research/lordsmstudy-2390.php> )

The clinical challenge

Colorectal cancer (CRC) is amongst the fourth commonest cancer worldwide 1 and is the second leading cause of cancer-related death in the UK 2. There are around 42,300 new colorectal cancer cases annually in the UK 3, while Scotland records over 3700 new cases 4. Liver metastases contributed to the death of approximately 50% of these patients 5.

Half of CRC patients develop liver metastasis 6. In Scottish liver centres, two-thirds of liver cancer surgery is for colorectal liver metastasis (CRLM). A Recent international survey demonstrated that almost all liver surgeons have experience with disappearing CRLM7.

Surgical resection remains the standard treatment for CRLM8. However, it is not always feasible without neoadjuvant chemotherapy 9. Most patients with CRLM receive chemotherapy 10 as the condition is often multiple 11, affects both lobes of the liver 12, and approximately half present with CRC present with a high systemic burden of the disease on their first presentation 6 .

Tumour response to chemotherapy has significantly improved, with up to 50% response rates for initially unresectable liver metastasis, of them 20% proceeding to liver resection with curative intent 13,14. Lesions disappear on radiological assessment in approximately half of the cases following chemotherapy 15,16. In subsequent investigations, this results in the disappearance of some or all metastatic diseases, a phenomenon termed *“disappearing liver metastases”* (dCRLM). ﻿The estimated affected population with dCRLM annually is approximately 360,000 cases globally. However, only a minority will have a complete pathological response (18% 17 to 25% 18) with the remainder (as high as 83%) having residual active cancer19. This poses a major therapeutic dilemma as most patients with a complete radiological response potentially still have residual disease. Indeed, there is a growing concern that the current observed rate of the pathologically viable tumour and rate of early recurrence is alarming 19. Preclinical studies suggested that surgery induces the growth of microscopic tumours 20, and in clinical practice, the dropout rates following the first stage hepatectomy for CRLM is strong support for the potential adverse effect of operating only on visible lesions 21. Therefore, not operating on those lesions may not be justified.

However, the area with viable cancer is substantially difficult to localize intraoperatively and often requires complex techniques and tools, which still have a suboptimal detection rate 22. Furthermore, many of these patients are subject to complications of extending the resection because of residual liver volume limitations 11,23 . Therefore, blind surgery has a significant risk of potential morbidity and mortality without guarantying improved outcome*.*

Some surgeons will, therefore, not offer surgery to these patients, while some advocate observation 24 and others endorse a surgical approach for all patients25.

The majority of CRLM are multiple, as previously mentioned, and when patients receive chemotherapy, most commonly, some of these lesions disappear, and some remain detectable. For this study and to provide a clear distinction, the situation where some lesions disappeared, and some remain detectable will be called mixed disappearing colorectal liver metastasis (mDLMs). Despite the literature addressing the CRLM, high quality studies address neither dCRLM nor mDLMs. A recent systematic review on the management of dCRLM identified low quality studies that require further validation albeit not addressing the fundamental question of this study 26. The fundamental question of this study is whether surgery is equivalent to observation in patients with multiple CRLM in whom some lesions disappeared and others remain detectable on preoperative imaging (mDLMs). Noteworthy the lack of clinical code specific to this condition and the reliance on routine health data did not show yield (communication with public health Scotland).

The approach

Concluded

Preliminary work:

Information gathering

&

Global engagement with the study

Collaborative engagement and appointing steering committee

Assessment of the need for a systematic review of literature

Survey of expert MDT attitudes on the management of specific case scenarios, inform the database design, reinforce engagement, and identify eligible centres

Development and refinement of database

Individual patient data collection in a secure database

Consensus conference and development of guidelines

Development of further research

Data collection and analysis

Translation into practice

**IRB and Caldicot approval**

The study has been awarded Caldicott approval through NHS Grampian Caldicott officer and registered as a UK wide study. Colleagues from outside the UK are encouraged to seek local approvals using the available documentations for this purpose.

**Proposed timeline for the data collection phase**

The study is currently open for data collection. <https://redcap.link/lords-m-register> follow the link to register and gain access to your database.

Timeline is subject to changes as dictated by the practical circumstances.

**The study team**

Having YOU and your team, we can have a better understanding on the best treatment of the disappeared colorectal liver metastasis.

**How to join?**

Register your interest here

Please fill out the [LORDS-M project registration form](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fredcap.link%2Flords-m-register&data=05%7C01%7Cmohamed.bekheit%40nhs.scot%7Cb7d08ec547a648e88f9008dabe748c80%7C10efe0bda0304bca809cb5e6745e499a%7C0%7C0%7C638031705028432574%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=WgBvBzsWPQvzoEuINzy6zRVwmXx51SN0rjtmrveC9G8%3D&reserved=0) to register your interest. Our administrators will then provide you with a REDCap account which can be used to submit your case files.

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**Your proposed team composition**

Each site PI is encouraged to choose additional 2 team members. Each site will have around 3 members and if more is required will be considered.

Although many cases would have been discussed in HPB MDT, there are many who have not gone through. You may want to liaise with colleagues who may have access to relevant patients records.

* Oncology team (e.g. oncologist, cancer nurse specialist),
* Pathology department (e.g. MDT pathologist for either CRC or HPB)
* Radiology department (e.g. Colorectal cancer or HPB radiologist)
* Colorectal surgical team

**Funding:**

The study is awarded funding for study manager, data curation and analysis.

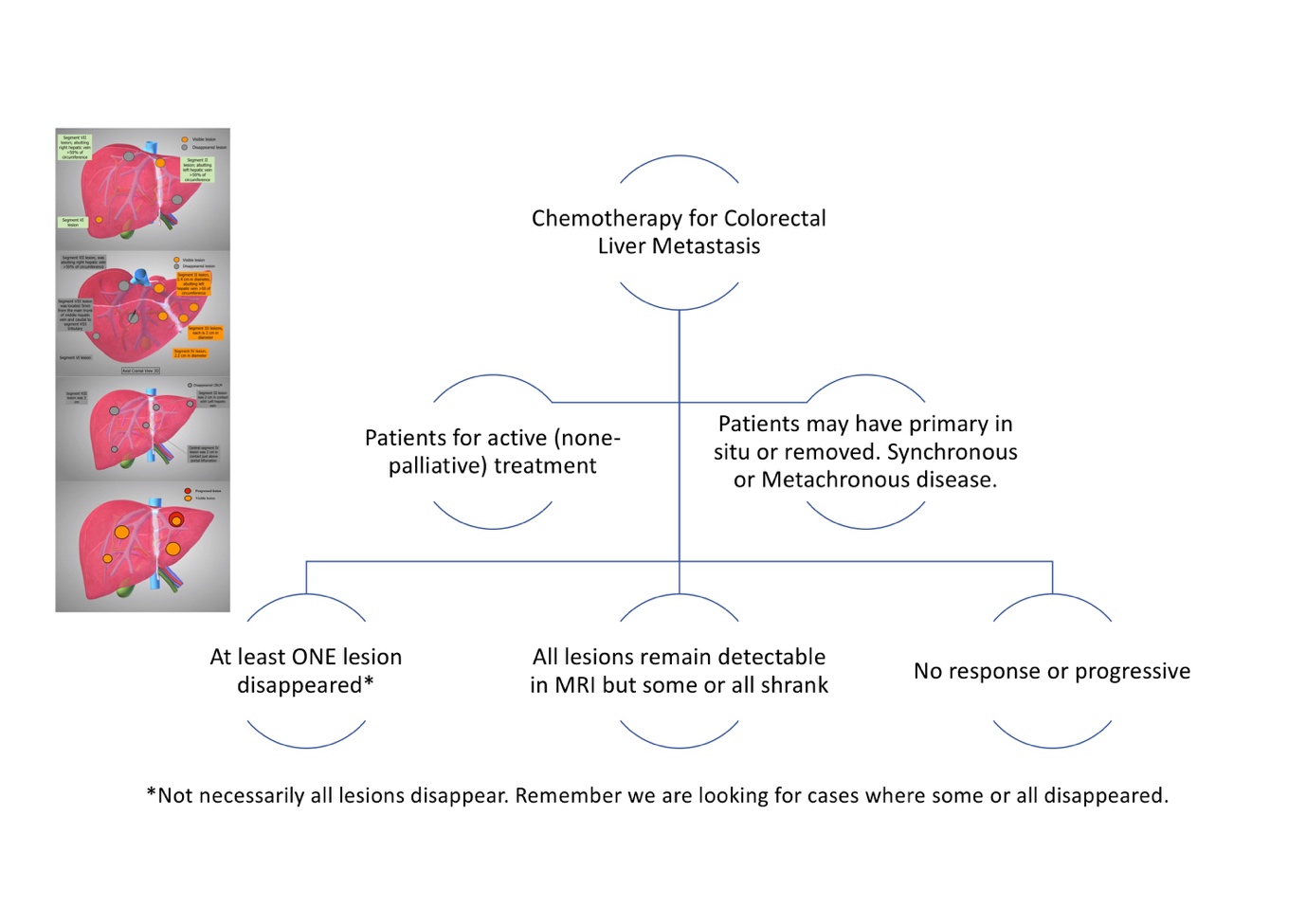
If you are contributing **from the UK**, you could claim (into your research fund) reimbursement for time utilised for submission of ***COMPLETE*** case records at £30 per hour (up to £45 per bundle [case + control]). There are additional reimbursement at the same rate for up to 20% of data quality check from a senior team member different from the members submitting the records.

Important clause: The reimbursement will be for cases of disappeared colorectal liver metastasis **AND** the control which will be case files for patient received chemotherapy with active treatment intent but have not had disappeared lesions.

**The information needed**

Standard information. The study collects standard information on patients who received chemotherapy for colorectal liver metastasis. Collection will include all ***prospective and retrospective from January 2017.***

Examples (zoom in to see)



**Authorship**

All site PIs will be included in named authorship (provided there are complete case records submitted by the centre). All other contributions will be acknowledged in collaborative authorship.

**Previous publications**

Nassar A, Cimpean S, Abdelhamid A, Jones RP, Wahba R, Fiorentini G, Aldrighetti L, Teh C, Alikhanov R, Hammond J, Silva M, Abdelmabod A, Truant S, Ferrero A, Sturesson C, Ahmed I, Ghazanfar M, Takemura N, Pawlik TM, Bekheit M. The dilemma of the disappeared colorectal liver metastasis: systematic review of reviews and evidence gap map. BJS Open. 2022 May 2;6(3):zrac051. doi: 10.1093/bjsopen/zrac051. PMID: 35598157; PMCID: PMC9124362.

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