

## COMMENTARY TO HABILITATION THESIS<sup>1</sup>

The incidence of cancer is increasing worldwide. Almost half of all cancers are diagnosed at the stage of regional or metastatic disease, which is associated with a worse prognosis as well as more demanding treatment. However, the hardship of treatment does not only involve significant patient discomfort caused by the diagnostic and therapeutic processes but also a greater financial burden on the health and social systems. The optimal method to divert the expected trend is to establish effective preventive measures that can influence the majority or, ideally, the entire population. These measures must be sufficiently cost-effective and sustainable, whilst retaining the highest degree of individualization.

To date, only a few validated biomarkers have been established and effectively used in cancer prevention. Their identification, testing, evaluation and implementation can take many years or even decades. A multidisciplinary collaboration is essential for the identification of relevant biomarkers and risk factors that will allow early recognition of individuals susceptible to cancer. In addition to researching biomarkers, primary prevention, and screening programs, society-wide debates should also focus on early and continuous public education, mental health promotion, as well as the inclusion of social factors in preventive measures.

This habilitation thesis primarily focuses on cancer prevention and the risk of second primary malignancies in cancer survivors. Due to early detection and advances in cancer treatment the number of these patients is steadily increasing. Approximately 20% of cancer survivors will experience another malignancy which, in more than half of the cases, becomes the cause of the patient's death. With respect to these advances in cancer care, secondary malignancies are becoming an important concern in survivorship care. In my original work, I aimed to identify the factors that may play a role in the development of second primary malignancies in colorectal cancer survivors. I evaluated the incidence of second neoplasia and the impact of comorbidities, medications, and the time from primary tumor diagnosis. Retrospective data were used to analyze these factors. In the first phase, 1174 patients with colorectal cancer who were diagnosed between 2003 and 2013 were evaluated, with follow-up to 2018 and a median follow-up of 10 years. We subsequently expanded the cohort by additional 227 patients, resulting in a total of 1401 patients. The period of diagnosis was extended to the interval 2003-2016, follow-up until 2020, with a median follow-up of 9 years. The results are summarized in the commentaries of the individual research papers. I am the lead author of the studies, I proposed the aim of the research, the methodology, and the design. I contributed significantly to the data collection and paper publication.

Using the model of colorectal cancer, I tried to outline the way in which cancer prevention can be personalized. Some works, such as chapters in books or Czech peer-reviewed journals, which are not commented on, but also other commented works, that are not related to colorectal cancer, are cited to illustrate the extent of my own contribution to the topic.

The risk of malignancy cannot be predicted by a single factor. Effective preventive therapy strategies will have to rely on comprehensive risk assessment tools for targeted intervention that are well balanced in terms of individualization and cost-effectiveness. Prevention cannot be regarded as a stand-alone medical discipline, but as a comprehensive strategy that accompanies a person from the premorbid period until the end of life.

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<sup>1</sup> The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

1. BOSSI, P, AT CHAN, L LICITRA, A TRAMA, E ORLANDI, EP HUI, J HALAMKOVA, S MATTHEIS, B BAUJAT, J HARDILLO, L SMEELE, C VAN HERPEN, A CASTRO, JP MACHIELS, ESMO GUIDELINES COMM, a EURACAN. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *ANNALS OF ONCOLOGY* [online]. 2021, **32**(4), 452–465. ISSN 0923-7534. Dostupné z: doi:[10.1016/j.annonc.2020.12.007](https://doi.org/10.1016/j.annonc.2020.12.007)

Document Type: Article; IF = 51,769; Quartile by IF: ONCOLOGY Q1; Quartile by AIS: ONCOLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	-	15	-

2. HALAMKOVA, J, T KAZDA, L PEHALOVA, R GONEC, S KOZAKOVA, L BOHOVICOVA, DA KRAKOROVA, O SLABY, R DEMLOVA, M SVOBODA a I KISS. Second primary malignancies in colorectal cancer patients. *SCIENTIFIC REPORTS* [online]. 2021, **11**(1). ISSN 2045-2322. Dostupné z: doi:[10.1038/s41598-021-82248-7](https://doi.org/10.1038/s41598-021-82248-7)

Document Type: Article; IF = 4, 997; Quartile by IF: MULTIDISCIPLINARY SCIENCES Q2; Quartile by AIS: MULTIDISCIPLINARY SCIENCES Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	100	90	100

3. HALAMKOVA, J *\*(corresponding author)\**, T KAZDA, L PEHALOVA, R GONEC, S KOZAKOVA, L BOHOVICOVA, O SLABY, R DEMLOVA, M SVOBODA a I KISS. The Impact of Diabetes Mellitus on the Second Primary Malignancies in Colorectal Cancer Patients. *FRONTIERS IN ONCOLOGY* [online]. 2021, **10**. ISSN 2234-943X. Dostupné z: doi:[10.3389/fonc.2020.573394](https://doi.org/10.3389/fonc.2020.573394)

Document Type: Article; IF = 5,738; Quartile by IF: ONCOLOGY Q2; Quartile by AIS: ONCOLOGY Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	100	90	100

4. HALAMKOVA, J, L BOHOVICOVA, L PEHALOVA, R GONEC, T STANEK, T KAZDA, L MOUKOVA, DA KRAKOROVA, S KOZAKOVA, M SVOBODA, R DEMLOVA a I KISS. Use of Hypolipidemic Drugs and the Risk of Second Primary Malignancy in Colorectal Cancer Patients. *CANCERS* [online]. 2022, **14**(7). ISSN 2072-6694. Dostupné z: doi:[10.3390/cancers14071699](https://doi.org/10.3390/cancers14071699)

Document Type: Article; IF = 6,575; Quartile by IF: ONCOLOGY Q1; Quartile by AIS: ONCOLOGY Q2 (data from 2021)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	100	80	100

5. PEHALOVA, L, D KREJCI, J HALAMKOVA, L SMARDOVA, L SNAJDROVA a L DUSEK. Significant current epidemiological trend: Haematological malignancies as subsequent primary tumours in cancer patients. *CANCER EPIDEMIOLOGY* [online]. 2021, **72**. ISSN 1877-7821. Dostupné z: doi:[10.1016/j.canep.2021.101929](https://doi.org/10.1016/j.canep.2021.101929)

Document Type: Article; IF = 2,89; Quartile by IF: ONCOLOGY Q4; Quartile by AIS: ONCOLOGY Q3

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	-	20	20

6. HALÁMKOVÁ, J. *\*(corresponding author)\** a M. PENKA. Current recommendations for the prevention and treatment of venous thromboembolism in cancer patients. *Klinická Onkologie* [online]. 2017, **30**(2), 100–105. Dostupné z: doi:[10.14735/amko2017100](https://doi.org/10.14735/amko2017100)

Document Type: Review; Category: ONCOLOGY; SJR Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	80	90	80

7. HALÁMKOVÁ, J. *\*(corresponding author)\**, D. ADÁMKOVÁ KRÁKOROVÁ a R. DEMLOVÁ. Anisocoria as a side effect of paclitaxel treatment. *Klinická Onkologie* [online]. 2021, **34**(4), 306–308. Dostupné z: doi:[10.48095/ccko2021306](https://doi.org/10.48095/ccko2021306)

Document Type: Article; Category: ONCOLOGY; SJR Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	100	80	100

8. HALAMKOVA, J *\*(corresponding author)\**, T KAZDA, D ADAMKOVA-KRAKOROVA, S RYBNICKOVA, I KISS a R DEMLOVA. Everolimus-related unilateral abdominal lymphedema in a

renal cancer patient A case report. *MEDICINE* [online]. 2020, **99**(42). ISSN 0025-7974. Dostupné z: doi:[10.1097/MD.00000000000022634](https://doi.org/10.1097/MD.00000000000022634)

**Document Type: Article; IF = 1,889; Quartile by IF: MEDICINE, GENERAL & INTERNAL Q3; Quartile by AIS: MEDICINE, GENERAL & INTERNAL Q3**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	100	90	100

9. **HALÁMKOVÁ, J. \*(corresponding author)\***, O. SLÁMA, D.A. KRÁKOROVÁ, R. DEMLOVÁ a J. KUŘE. Communication with cancer patient. *Vnitřní Lekarství*. 2019, **65**(5), 359–362.

**Document Type: Article; Category: CARDIOLOGY + INTERNAL MEDICINE; SJR Q4**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	90	90	-

10. WIND, A, ED HARTMAN, RRJP VAN EEKEREN, RPWF WIJN, J HALAMKOVA, J MATTSON, S SIESLING a WH VAN HARTEN. Validating a generic cancer consumer quality index in eight European countries, patient reported experiences and the influence of cultural differences. *BMC CANCER* [online]. 2021, **21**(1). ISSN 1471-2407. Dostupné z: doi:[10.1186/s12885-021-07943-0](https://doi.org/10.1186/s12885-021-07943-0)

**Document Type: Article; IF = 4,638; Quartile by IF: ONCOLOGY Q1; Quartile by AIS: ONCOLOGY Q2**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	-	20	10

11. **HALAMKOVA, J \*(corresponding author)\***, I KISS, Z PAVLOVSKY, J JARKOVSKY, J TOMASEK, S TUCEK, L HANAKOVA, M MOULIS, Z CECH, J ZAVRELOVA a M PENKA. Clinical Relevance of uPA, uPAR, PAI 1 and PAI 2 Tissue Expression and Plasma PAI 1 Level in Colorectal Carcinoma Patients. *HEPATO-GASTROENTEROLOGY* [online]. 2011, **58**(112), 1918–1925. ISSN 0172-6390. Dostupné z: doi:[10.5754/hge10232](https://doi.org/10.5754/hge10232)

Document Type: Article; IF = 0,658; Quartile by IF: GASTROENTEROLOGY & HEPATOLOGY Q4; Quartile by AIS: GASTROENTEROLOGY & HEPATOLOGY 0

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	100	90	100

12. KRAKOROVA, DA, J HALAMKOVA *\*(corresponding author)\**, S TUCEK, O BILEK, J KRISTEK, T KAZDA, IS ZAMBO, R DEMLOVA a I KISS. Penis as a primary site of an extraskeletal Ewing sarcoma A case report. *MEDICINE* [online]. 2021, **100**(11). ISSN 0025-7974. Dostupné z: doi:[10.1097/MD.00000000000025074](https://doi.org/10.1097/MD.00000000000025074)

Document Type: Article; IF = 1,817; Quartile by IF: MEDICINE, GENERAL & INTERNAL Q3; Quartile by AIS: MEDICINE, GENERAL & INTERNAL Q3

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	80	50	-