



Intake of red and processed meat on the incidence of cancer: Are the risks really relevant?



The conclusions of a meeting aimed at evaluating the carcinogenicity of the consumption of red meat and processed meat, which was held in October of 2015 at the International Agency for Research on Cancer in Lyon (France), were published in December 2015 (Bouvard et al., 2015). Twenty-two scientists (Working Group) from 10 different countries participated in that meeting. These scientists assessed more than 800 epidemiological studies on the association of cancer with the consumption of red meat and processed meats. The Working Group classified the consumption of processed meats as carcinogenic to humans (Group 1) and the consumption of red meat as probably carcinogenic to humans (Group 2A). Extensive details on the evaluations, as well as the consequent decisions, were published in 2018: Red Meat and Processed Meat, IARC Monographs on the Evaluation and Carcinogenic Risks to Humans, Volume 114.

In 2017, we published in this Journal a short-review (Domingo and Nadal, 2017) covering the scientific articles published between October 2015 and February 2017. Between February 2017 and today, a number of investigations on the carcinogenicity of consumption of red meat and/or processed meats have joined the already exhaustive scientific literature. The results of the studies by De Vries et al. (2017), Alsherdah and Akhtar (2018), Behrens et al. (2018), Mafiana et al. (2018), Salter (2018), Bradbury et al. (2019), Czaderny (2019), Ganjavi and Faraji (2019), Imad et al. (2019), Lourenço et al. (2018) and Saliba et al. (2019), have all agreed -to a greater or lesser extent-that the consumption of red and processed meat is associated with an increased risk of colorectal cancer (CRC). Various recent reviews have also corroborated the IARC decision (Fardet et al., 2017; van Zutphen et al., 2017; Givens, 2018; Zhao et al., 2019), mainly with respect to the risks of CRC. In contrast, only a few studies have not reached the same conclusion. Thus, Ruan et al. (2019) only found a small -but meaningful-cancer burden associated with red and processed meat consumption, while Pramual et al. (2018) did not find an association between a positive fecal immunochemical test and meat consumption.

On the other hand, since our previous review (Domingo and Nadal, 2017), a number of studies have investigated potential mechanisms for cancer risks derived from the consumption of red and processed meats. It has been suggested that DNA adduct formation can contribute to red meat related CRC risk (Hemeryck et al., 2018), while the frequency of red meat intake (in non-smokers) increases the risk of CRC in the case of GST gene polymorphisms (Klusek et al., 2019). The potential role played by environmental factors and gut microbiota (Song and Chan, 2019), as well as the gene polymorphisms of metabolic enzymes (Doaei et al., 2018) has been discussed. The role of certain chemical substances such as heterocyclic aromatic amines and polycyclic aromatic hydrocarbons, formed during the heating process of meats, and that of N-nitroso compounds, formed during the curing of meats, has been also investigated and discussed (Chiang and Quek, 2017; Domingo, 2017;

Jeyakumar et al., 2017; Kruger and Zhou, 2018; Turesky, 2018; González et al., 2019; Khosravi-Darani et al., 2019). Another possible reason for the association between red meat consumption and CRC could be the adverse effects exerted by the heme iron contained in red meat, which would promote the formation of mutagenic and carcinogenic agents by affecting homeostasis and colonic epithelial cell renewal (Kruger and Zhou, 2018; Sasso and Latella, 2018a,b).

In contrast to the above evidences, in October 1, 2019, the journal Annals of Internal Medicine has published a series of 5 review-articles focused on the possible effect of red and processed meat on the incidence of cancer and cardiometabolic diseases. These publications are part of NutriRECs (Nutritional Recommendations and accessible Evidence summaries Composed of Systematic reviews), the goal of which is to develop trustworthy guideline recommendations on nutrition (Johnston et al., 2018, 2019). Three of these reviews were specifically focused on cancer. The main conclusions were the following: “the possible absolute effects of red and processed meat consumption on cancer mortality and incidence are very small, and the certainty of evidence is low to very low” (Han et al., 2019); “low- or very-low-certainty evidence suggests that dietary patterns with less red and processed meat intake may result in very small reductions in adverse cardiometabolic and cancer outcomes” (Vernooij et al., 2019), and “low-to very-low-certainty evidence suggests that diets restricted in red meat may have little or no effect on major cardiometabolic outcomes and cancer mortality and incidence” (Zeraatkar et al., 2019). Based on this, anyone could think that the recent recommendations on the reduction of the intake of red and processed meats are unnecessary, as the benefits on the prevention of cancer (mainly CRC, but also stomach and others) would be rather irrelevant.

The conclusions of these very recent reviews have immediately reached the generalist media. As usual on health issues, there is nothing worse for the public opinion in general, and for family doctors and specialists in particular, receive such contradictory messages. We must expect that the IARC -and other international organisms-will give a prompt and conclusive clarifying response to this.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Alsherdah, N., Akhtar, S., 2018. Diet, obesity and colorectal carcinoma risk: results from a national cancer registry-based middle-eastern study. *BMC Canc.* 18 (1), 1227. <https://doi.org/10.1186/s12885-018-5132-9>.
- Behrens, G., Gredner, T., Stock, C., Leitzmann, M.F., Brenner, H., Mons, U., 2018. *Cancers*

<https://doi.org/10.1016/j.fct.2019.110884>

- due to excess weight, low physical activity, and unhealthy diet. *Dtsch. Arztebl. Int.* 115 (35–36), 578–585.
- Bouvard, V., Loomis, D., Guyton, K.Z., Grosse, Y., Ghisassi, F.E., Benbrahim-Tallaa, L., Guha, N., Mattock, H., Straif, K., International Agency for Research on Cancer Monograph Working Group, 2015. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 16 (16), 1599–1600.
- Bradbury, K.E., Murphy, N., Key, T.J., 2019. Diet and colorectal cancer in UK Biobank: a prospective study. *Int. J. Epidemiol.* <https://doi.org/10.1093/ije/dyz064>. pii: dyz064.
- Chiang, V.S., Quek, S.Y., 2017. The relationship of red meat with cancer: effects of attributable fractions for colorectal cancer and red and processed meats in Colombia - a macro-simulation study. *Colomb. Méd.* 48 (2), 64–69.
- Doaei, S., Hajiesmaeil, M., Aminifard, A., Mosavi-Jarrahi, S.A., Akbari, M.E., Gholamalizadeh, M., 2018. Effects of gene polymorphisms of metabolic enzymes on the association between red and processed meat consumption and the development of colon cancer; a literature review. *J. Nutr. Sci.* 7, e26. <https://doi.org/10.1017/jns.2018.17>.
- Domingo, J.L., 2017. Concentrations of environmental organic contaminants in meat and meat products and human dietary exposure: a review. *Food Chem. Toxicol.* 107 (Pt A), 20–26.
- Domingo, J.L., Nadal, M., 2017. Carcinogenicity of consumption of red meat and processed meat: a review of scientific news since the IARC decision. *Food Chem. Toxicol.* 105, 256–261.
- Fardet, A., Druesne-Pecollo, N., Touvier, M., Latino-Martel, P., 2017. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. *Crit. Rev. Oncol. Hematol.* 119, 94–112.
- Ganjavi, M., Faraji, B., 2019. Late effect of the food consumption on colorectal cancer rate. *Int. J. Food Sci. Nutr.* 70 (1), 98–106.
- Givens, D.I., 2018. Review: dairy foods, red meat and processed meat in the diet: implications for health at key life stages. *Animal* 12 (8), 1709–1721.
- González, N., Marqués, M., Nadal, M., Domingo, J.L., 2019. Occurrence of environmental pollutants in foodstuffs: a review of organic vs. conventional food. *Food Chem. Toxicol.* 125, 370–375.
- Han, M.A., Zeraatkar, D., Guyatt, G.H., Vernooij, R.W.M., El Dib, R., Zhang, Y., Algarni, A., Leung, G., Storman, D., Valli, C., Rabassa, M., Rehman, N., Parvizian, M.K., Zworh, M., Bartoszko, J.J., Lopes, L.C., Sit, D., Bala, M.M., Alonso-Coello, P., Johnston, B.C., 2019 Oct 1. Reduction of red and processed meat intake and cancer mortality and incidence: a systematic review and meta-analysis of cohort studies. *Ann. Intern. Med.* <https://doi.org/10.7326/M19-0699>.
- Hemeryck, L.Y., Rombouts, C., De Paepe, E., Vanhaecke, L., 2018. DNA adduct profiling of in vitro colonic meat digests to map red vs. white meat genotoxicity. *Food Chem. Toxicol.* 115, 73–87.
- Imad, F.E., Drissi, H., Tawfiq, N., Bendahhou, K., Jouti, N.T., Benider, A., Radallah, D., 2019. Epidemiological, nutritional and anatomopathological features of patients with colorectal cancer in the greater Casablanca region. *Pan. Afr. Med. J.* 32, 56 (in French).
- Jeyakumar, A., Dissabandara, L., Gopalan, V., 2017. A critical overview on the biological and molecular features of red and processed meat in colorectal carcinogenesis. *J. Gastroenterol.* 52 (4), 407–418.
- Johnston, B.C., Alonso-Coello, P., Bala, M.M., Zeraatkar, D., Rabassa, M., Valli, C., Marshall, C., El Dib, R., Vernooij, R.W.M., Vandvik, P.O., Guyatt, G.H., 2018. Methods for trustworthy nutritional recommendations NutriRECS (Nutritional Recommendations and accessible Evidence summaries Composed of Systematic reviews): a protocol. *BMC Med. Res. Methodol.* 18 (1), 162.
- Johnston, B.C., Zeraatkar, D., Han, M.A., Vernooij, R.W.M., Valli, C., El Dib, R., Marshall, C., Stover, P.J., Fairweather-Taitt, S., Wójcik, G., Bhatia, F., de Souza, R., Brotons, C., Meerpohl, J.J., Patel, C.J., Djulbegovic, B., Alonso-Coello, P., Bala, M.M., Guyatt, G.H., 2019 Oct 1. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the nutritional recommendations (NutriRECS) consortium. *Ann. Intern. Med.* <https://doi.org/10.7326/M19-1621>.
- Khosravi-Darani, K., Barzegar, F., Baghdadi, M., 2019. Detoxification of heterocyclic aromatic amines by probiotic to inhibit medical hazards. *Mini Rev. Med. Chem.* <https://doi.org/10.2174/1389557519666190318102201>.
- Klusek, J., Nasierowska-Guttmejer, A., Kowalik, A., Wawrzycska, I., Chrapek, M., Lewitowicz, P., Radowicz-Chil, A., Klusek, J., Gluszek, S., 2019. The influence of red meat on colorectal cancer occurrence is dependent on the genetic polymorphisms of S-glutathione transferase genes. *Nutrients* 11 (7), E1682. <https://doi.org/10.3390/nu11071682>.
- Kruger, C., Zhou, Y., 2018. Red meat and colon cancer: a review of mechanistic evidence for heme in the context of risk assessment methodology. *Food Chem. Toxicol.* 118, 131–153.
- Lourenço, S., Gunge, V.B., Andersson, T.M., Andersen, C.L.E., Lund, A.Q., Køster, B., Hansen, G.L., 2018. Avoidable colorectal cancer cases in Denmark - the impact of red and processed meat. *Canc. Epidemiol.* 55, 1–7.
- Mafiana, R.N., Al Lawati, A.S., Waly, M.I., Al Farsi, Y., Al Kindi, M., Al Moundhri, M., 2018. Association between dietary and lifestyle indices and colorectal cancer in Oman: a case-control study. *Asian Pac. J. Cancer Prev. APJCP* 19 (11), 3117–3122.
- Pramual, P., Sarakarn, P., Kamsa-ard, S., Sirapornkul, C., Maneenin, N., Thavondunstid, P., Juntarach, P., Promthet, S., 2018. Lack of association between red meat consumption and a positive fecal immunochemical colorectal cancer screening test in khon kaen, Thailand: a population-based randomized controlled trial. *Asian Pac. J. Cancer Prev. APJCP* 19 (1), 271–278.
- Ruan, Y., Poirier, A.E., Hebert, L.A., Grevers, X., Walter, S.D., Villeneuve, P.J., Brenner, D.R., Friedenreich, C.M., ComPARE Study Team, 2019. Estimates of the current and future burden of cancer attributable to red and processed meat consumption in Canada. *Prev. Med.* 122, 31–39.
- Saliba, W., Rennett, H.S., Gronich, N., Gruber, S.B., Rennett, G., 2019. Red meat and processed meat intake and risk of colorectal cancer: a population-based case-control study. *Eur. J. Cancer Prev.* 28 (4), 287–293.
- Salter, A.M., 2018. The effects of meat consumption on global health. *Rev. Sci. Tech.* 37 (1), 47–55.
- Sasso, A., Latella, G., 2018a. Dietary components that counteract the increased risk of colorectal cancer related to red meat consumption. *Int. J. Food Sci. Nutr.* 69 (5), 536–548.
- Sasso, A., Latella, G., 2018b. Role of heme iron in the association between red meat consumption and colorectal cancer. *Nutr. Cancer* 70 (8), 1173–1183.
- Song, M., Chan, A.T., 2019. Environmental factors, gut microbiota, and colorectal cancer prevention. *Clin. Gastroenterol. Hepatol.* 17 (2), 275–289.
- Turesky, R.J., 2018. Mechanistic evidence for red meat and processed meat intake and cancer risk: a follow-up on the international agency for research on cancer evaluation of 2015. *Chimia* 72 (10), 718–724.
- van Zutphen, M., Kampman, E., Giovannucci, E.L., van Duijnhoven, F.J.B., 2017. Lifestyle after colorectal cancer diagnosis in relation to survival and recurrence: a review of the literature. *Curr. Colorectal Canc. Rep.* 13 (5), 370–401.
- Vernooij, R.W.M., Zeraatkar, D., Han, M.A., El Dib, R., Zworh, M., Milio, K., Sit, D., Lee, Y., Gomaa, H., Valli, C., Swierz, M.J., Chang, Y., Hanna, S.E., Brauer, P.M., Sievenpiper, J., de Souza, R., Alonso-Coello, P., Bala, M.M., Guyatt, G.H., Johnston, B.C., 2019 Oct 1. Patterns of red and processed meat consumption and risk for cardiometabolic and cancer outcomes: a systematic review and meta-analysis of cohort studies. *Ann. Intern. Med.* <https://doi.org/10.7326/M19-1583>.
- Zeraatkar, D., Johnston, B.C., Bartoszko, J., Cheung, K., Bala, M.M., Valli, C., Rabassa, M., Sit, D., Milio, K., Sadeghirad, B., Agarwal, A., Zea, A.M., Lee, Y., Han, M.A., Vernooij, R.W.M., Alonso-Coello, P., Guyatt, G.H., El Dib, R., 2019 Oct 1. Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes: a systematic review of randomized trials. *Ann. Intern. Med.* <https://doi.org/10.7326/M19-0622>.
- Zhao, Z., Wang, F., Chen, D., Zhang, C., 2019. Red and processed meat consumption and esophageal cancer risk: a systematic review and meta-analysis. *Clin. Transl. Oncol.* <https://doi.org/10.1007/s12094-019-02157-0>.

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