sustainability

MDPI

Review

Productivity-Enhancing Technologies. Can Consumer Choices Affect the Environmental Footprint of Beef?

Isaac A. Aboagye [1,2], Marcos R. C. Cordeiro [1,2], Tim A. McAllister [3] and Kim H. Ominski [1,2,*]

1 Department of Animal Science, University of Manitoba, 201-12 Dafoe Road, Winnipeg, MB R3T 2N2, Canada; isaac.aboagye@umanitoba.ca (I.A.A.); Marcos.Cordeiro@umanitoba.ca (M.R.C.C.)
2 National Centre for Livestock and the Environment, Winnipeg, MB R3T 2N2, Canada
3 Lethbridge Research and Development Center, Agriculture and Agri-Food Canada, Lethbridge, AB T1J 4B1, Canada; tim.mcallister@canada.ca
* Correspondence: Kim.Ominski@umanitoba.ca

Abstract: Use of productivity-enhancing technologies (PET: growth hormones, ionophores, and beta-adrenergic agonists) to improve productivity has recently garnered public attention regarding environmentally sustainability, animal welfare, and human health. These consumer perceptions and increased demand for PET-free beef offer opportunities for the beef industry to target niche premium markets, domestically and internationally. However, there is a need to critically examine the trade-offs and benefits of beef raised with and without the use of PETs. This review contains a summary of the current literature regarding PET products available. The implications of their use on resource utilization, food safety and security, as well as animal health and welfare are discussed. Furthermore, we identified gaps in knowledge and future research questions related to the sustainability of these technologies in beef production systems. This work highlights the tradeoffs between environmental sustainability of beef and supplying the dietary needs of a growing population.

Keywords: productivity-enhancing technologies; environment sustainability; land use; water use; greenhouse gas; beef cattle

Citation: Aboagye, I.A.; Cordeiro, M.R.C.; McAllister, T.A.; Ominski, K.H. Productivity-Enhancing Technologies. Can Consumer Choices Affect the Environmental Footprint of Beef? *Sustainability* **2021**, *13*, 4283. https://doi.org/10.3390/su13084283

Academic Editor: Flavio Boccia

Received: 10 March 2021
Accepted: 8 April 2021
Published: 12 April 2021

1. Introduction

It is estimated that the human world population will exceed nine billion by 2050 [1], raising a global concern over food security, especially in developing countries. Increasing consumption of animal protein has been suggested as one of the sustainable strategies to address food security, especially for the nearly 800 million people in the world who subsist on less than US$ 2.0 a day [2]. Globally, of the 60 g of daily protein intake recommended for an adult (>18 years and 75 kg [3]), approximately one third is acquired from animal protein [4]. Animal protein is a rich source of the most commonly limiting essential amino acids, including leucine, methionine, and lysine [5–7], as well as vitamin B12 [8], calcium [9], and heme-iron [10]. Furthermore, animal protein is generally more digestible and the amino acids more bioavailable due to the absence of the anti-nutritional factors associated with plant-based proteins [11–13].

Despite these benefits, the potential of animal agriculture to feed a growing population has been questioned over environmental concerns, including the use of 30% of the global arable land for feed production, 32% of the world's freshwater [14], and production of 14.5% of global greenhouse gas emissions (GHG [15]). Beef cattle production has been deemed to be the most environmentally unsustainable among the major livestock production systems [16] as its land, water, and carbon footprints are 28-, 11-, and five-fold higher, respectively, than pork or chicken production [17]. However, studies in Brazil [18], Australia [19], United States (US [20]), and Canada [21,22] have demonstrated that modern intensive cattle production has lowered the environmental footprint of beef production on an intensity basis, as result of reductions in land and water use, as well as GHG emissions.

The beef production systems in these countries usually involve transitioning animals from a cow–calf system (cow herd produces calves) to a backgrounding system (weaned calves fed forage-based diets) and then to finishing diets (steers/heifers, fed high-energy grain-based diets), prior to being sent to a processor or packer. Use of productivity-enhancing technologies (PET) in these "conventional" production systems has been adopted to improve productivity [23] and may reduce the environmental footprint. Cattle operations not using PETs are often referred to as "natural" production systems. Growth-enhancing technologies include implants, estrous suppressants, beta-adrenergic agonists (βAA), and ionophores [23].

Despite demonstrated benefits in productivity, consumers perceive that PETs may have negative impacts on the environment, food safety, and animal welfare [24–26]. As a result, more than half of consumers participating in a global internet survey declared that they preferred meat and other animal food products from beef cattle that did not receive growth implants or antibiotics [27]. These online responses may contain inherent biases, as they were based on claimed behavior rather than direct measurement of product preferences within the food service and the retail sectors.

This review describes the use of PETs in beef production systems, consumer perceptions and preferences regarding their use, and their potential impacts on the environment.

2. Productivity-Enhancing Technologies in Beef Production

Globally, many PETs such as hormones and ionophores have been used in beef for more than 60 years, while other approved products such as βAA have only been approved within the last few decades (Table 1 [28,29]).

Table 1. Productivity-enhancing technologies commonly used in beef production.

Class [a]	Mode of Action	Substance [b]	Mode of Administration
Growth hormones			
Endogenous/Synthetic	Increase protein deposition at the expense of fat to increase growth rate and decrease amount of feed required for the animal to gain weight.	Estradiol-17β, Testosterone, Progesterone/Zearalenone, Trenbolone acetate	Implants
		Melengestrol acetate	In-Feed
Beta-adrenergic agonists	Redirect nutrients from digestive organs into muscle tissue, thus increasing muscle mass accretion at the expense of fat deposition.	Ractopamine chloride, Zilpaterol chloride	In-Feed
Antibiotics [c]			
Ionophores	Act against Gram-positive bacteria by altering membrane permeability to promote propionate formation in the rumen, which is more energetically favorable than acetate production.	Monensin, Lasalocid, Salinonmycin	In-Feed
Macrolides Aminoglycosides	Has bacteriostatic effect on both Gram-positive and Gram-negative bacteria, thus reducing microbial competition for nutrients.	Tylosin, Neomycin	In-Feed, water, or parenteral
Tetracyclines		Oxytetracycline, Chlortetracyclic	

[a] Used in growth promotion by beef producing countries, including countries in North America (US, Canada, Mexico), Australian–New Zealand region, South America (Brazil and Argentina), and Africa (South Africa). Approval of specific products depends on the regulatory framework within each country. [b] Synthetic derivatives of estrogen, testosterone, and progesterone are zearalenone, trenbolone acetate, and melengesterol acetate, respectively. [c] Globally not recommended for feed efficiency, except ionophores. However, implementation is subject to local and national legislation or regulation.

2.1. *Hormonal Implants*

In cattle, hormones are naturally produced by the anterior pituitary gland, thyroid, adrenal cortex, testes, and ovaries [30], influencing reproduction, growth, and development [31]. Natural reproductive hormones (i.e., estradiol-17β (E), testosterone, and progesterone) and synthetic derivatives including zearalenone (Z: estrogen), trenbolone acetate (TBA: testosterone), and melengestrol acetate (MGA: progesterone) are used in beef production [32]. With the exception of MGA, which is administered in the feed, growth hormones are dispensed as implant pellets, which are placed between the skin and the cartilage of the ear [33]. Active agents within growth implants are embedded within a matrix (compressed or silicon rubber), which releases the promotant into the bloodstream over a period of 60 to 120 days [29].

A meta-analysis of 34 studies by Reinhardt and Wagner [34] found that implants increased weight gain and carcass weight by 0.27 kg/d and 21.4 kg, respectively. In the backgrounding and finishing phases, implanted cattle fed diets containing grain gained from 10% to 30% more than those that were not implanted [34–36]. Furthermore, implants can increase dry matter (DM) intake in cattle by 5% to 10% and feed efficiency by 5% to 15% [37]. Growth hormones can be used at any stage of the production system, but the type of implant used is often selected based on the stage of production (i.e., from suckling through to weaning, backgrounding, and finishing phases [38]). An individual animal can receive up to three implants over the duration of the production cycle. There is no withdrawal time if the implant is administered at the correct time, as the hormone is absorbed into the bloodstream and fully expended prior to slaughter [39].

2.2. Ionophores

Ionophores are carboxylic polyether antibiotics and include products such as monensin (MON), lasalocid, salinomycin, and laidlomycin [40]. Ionophores function by selecting against Gram-positive bacteria and rumen protozoa [41]. Furthermore, ionophores promote the formation of propionate in the rumen, which acts as an electron sink and reduces the availability of electrons for the reduction of carbon dioxide to methane by methanogens [41]. Ionophores can also reduce DM intake (DMI) by 3% to 7.5%, while maintaining weight gain, resulting in 5.6% to 7.5% improvement in feed efficiency [42–45]. They are usually administered to cattle in confinement during the growing and finishing phases and do not require withdrawal prior to slaughter [46].

2.3. Beta-Adrenergic Agonists

Another class of growth promotants used in the beef cattle industry are βAA, which include ractopamine chloride (RC) and zilpaterol chloride (ZC) [47]. Beta-adrenergic agonists mimic adrenalin, redirecting nutrients from digestive organs into muscle tissue, thereby increasing muscle mass at the expense of fat synthesis [48].

A meta-analysis including data from up to 50 studies showed that RC increased weight gain by 0.24 kg/d and carcass weight by 7.3 kg [49]. Similarly, ZC increased weight gain by 0.15 kg/d, and final body and carcass weights by 8 and 15 kg, respectively [49]. Beta-adrenergic agonists are mainly fed to cattle during the last 20 to 42 days of the finishing phase, depending on the type of βAA [33,50]. Ractopamine chloride is fed for 28 to 42 days with no withdrawal, while ZC is fed for 20 to 40 days with a three-day withdrawal prior to slaughter [50].

Use of PETs can reduce the cost of production. For example, in the US, the cost of gain in PET-treated cattle during the finishing phase was reduced by 6% to 25% compared to PET-free cattle when feed was priced at US$ 0.26/kg DM, and the cost of gain was US$ 2.20/kg [45,51,52]. Furthermore, producers that use PETs do not have the costs associated with the arduous record keeping and auditing procedures required in "natural" production systems [52].

3. The Role of PETs in Global Beef Production

Differences in the regulatory framework among countries regarding the use of PETs not only impacts domestic production, but can also create non-tariff barriers to export. The use of PETs is permitted in North America (US, Canada, and Mexico) and Australia–New Zealand [53], which produced 20% (13.5 million tonnes: Mt) and 4% (2.9 Mt), respectively, of total global beef in 2018 (67.4 Mt [54]). Brazil and Argentina, which also supplied 15% (9.9 Mt) and 5% (3.1 Mt), respectively, of the global beef market in 2018 [54] also allow the use of PETs [55]. All of the above countries rely heavily on export markets and therefore must meet requirements of those countries that do not allow use of PETs, including the European Union (EU), China, and Russia [33], which collectively produced 27% of global beef in 2018 (i.e., 10.6, 5.8, and 1.6 Mt, respectively [54]).

4. Impact of PET Use on Consumer Choice

Global per capita beef consumption ranges from 0.5 to 40 kg, with an average consumption of 6.4 kg in 2018 [56]. Consumption is influenced by many factors, including management practices (use of PETs), culture, palatability, appearance, and price [57]. The demand for beef and beef products raised without the routine use of PET and labeled as "raised without antibiotics", "raised without added hormones", "natural" (raised without antibiotics and additional hormones), "organic" (raised without antibiotics and additional hormones and feed that was not genetically engineered or produced using synthetic fertilizer), or "100% grass-fed" is growing, but still only constitutes a small portion of the total market as depicted in Figures 1 and 2 [58–60]. The increase in consumer demand for beef raised without PET has increased the number of feedlot operators registered in "natural" programs in some regions of the US. From 2010 to 2018, the percentage of the 36,856 Texas beef producers enrolled in "natural" programs (i.e., raised without antibiotics and additional hormones) increased from 35% to 43%, while those enrolled in "raised without added hormone" programs increased from 5.2% to 23.8% (Figure 3 [61]). A study conducted by Nielsen Global Health and Ingredient–Sentiment Survey [27] with 30,000 online consumers from 69 countries indicated that the majority of the respondents from Europe (65%), Latin America (59%), Asia-Pacific (59%), Africa/Middle East (55%), and North America (54%) would avoid animal products containing hormones or antibiotics. Although online survey methodology allows for global outreach, it provides the sentiments of only existing internet users and not the total population. Again, because this survey was based on claimed behavior rather than verified measured data from abattoirs, wholesalers, hotels, restaurants, and grocery stores, biases may not truly represent the market trends in terms of types and volumes of animal products sold. Respondents may also not have a complete understanding as to how these additives are used in the industry and the regulatory oversight for their use. Furthermore, they also likely do not recognize the reduction in retail price associated with the use of PETs, which was estimated to lower the cost of US beef from US$ 15.50 to 13.80/kg [62].

In the US, labeling beef as "raised without antibiotics or hormones" can increase its price by as much as US$ 6.56/kg, a 47% premium over conventionally produced beef US$14.06/kg [63]. Similarly, in Canada, a recent study of consumers' willingness to pay premiums for beef products labeled as "use of antibiotics with no hormones", "responsible use of antibiotics with hormones", "responsible use of antibiotics with no hormones", and "no antibiotics and no hormones" reported that they had dollar premiums/kg of beef product at $12.13, $14.22, $21.08, and $30.07 CAD, respectively [64]. Lewis et al. [65] also examined willingness of European consumers to pay a premium when the average beef price was 18.27€/£ per kg and showed that German and British consumers would pay 29% and 20% more, respectively, for PET-free beef. Furthermore, in Argentina, Colella, and Ortega, [66] showed that consumers that purchase from a supermarket were willing to pay a premium of (US$ 2.5/kg) for certified "organic" beef as compared to consumers that were purchasing unverified beef from a local butcher. Willingness to pay more for "natural" or "organic" beef is attributed to concerns over the environment, animal welfare, and food safety [24,26,57,65]. Even though some consumers may express concerns about PET use or preference for PET-free beef when interviewed, at the purchasing point, other attributes such as price largely determine their purchasing behavior [57].

Recently, Hirvonen et al. [67] showed that meat products were more affordable for high-income nations such as Australia, New Zealand, Europe, and North America than low-income countries in South Asia and sub-Saharan Africa. Therefore, globally, the willingness to pay a premium for PET-free beef is likely heavily influenced by consumer income. Such a premium is unlikely to be a viable option for those who live on less than US$ 2.0/day in low-income countries, even though these populations are likely to realize the greatest nutritional benefit as a result of including meat in their diets.

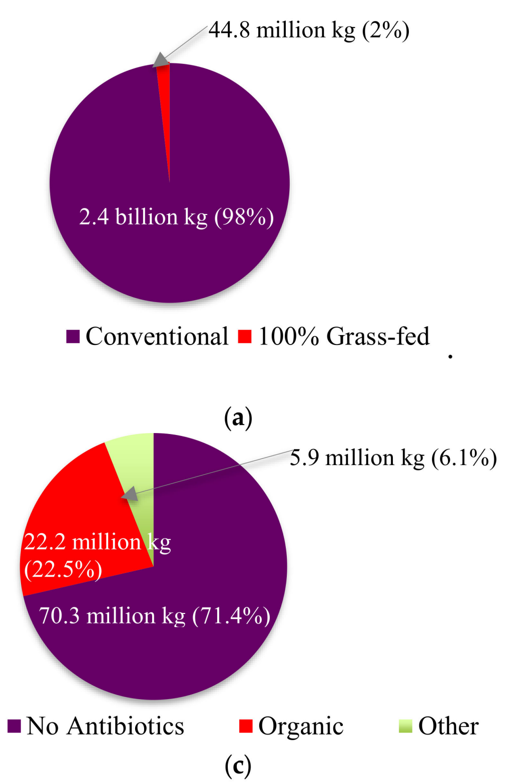

Figure 1. Volume of US retail beef sold in 2019 by (**a**) production ("conventional" vs. "100% grass-fed"); (**b**) total claims (without claim vs. claim); and (**c**) type of claim ("no antibiotic" vs. "organic" vs. other (e.g., Halal, Kosher or Kobe-Style)). Source: Modified from Beef [58].

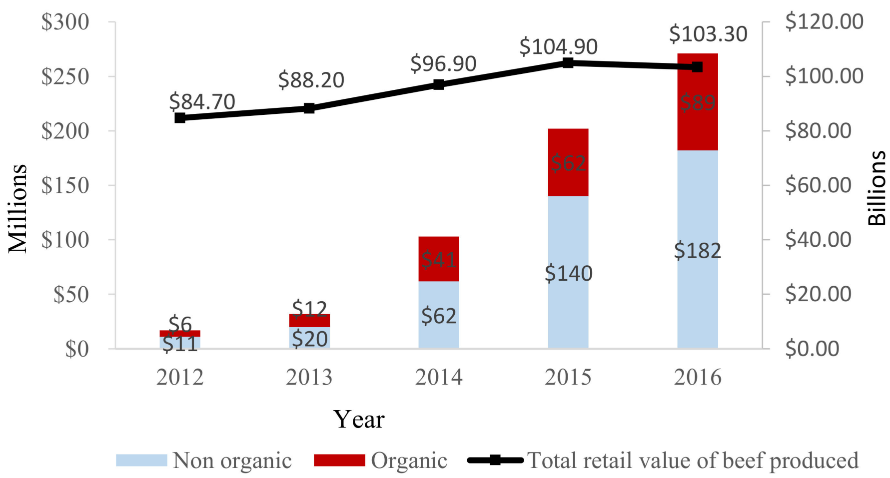

Figure 2. Total retail value (billions), "organic" and non-organic "grass-fed" beef retail sales (millions) from 2012 to 2016 in US. Source: Modified from Cheung et al. [59]; USDA [60].

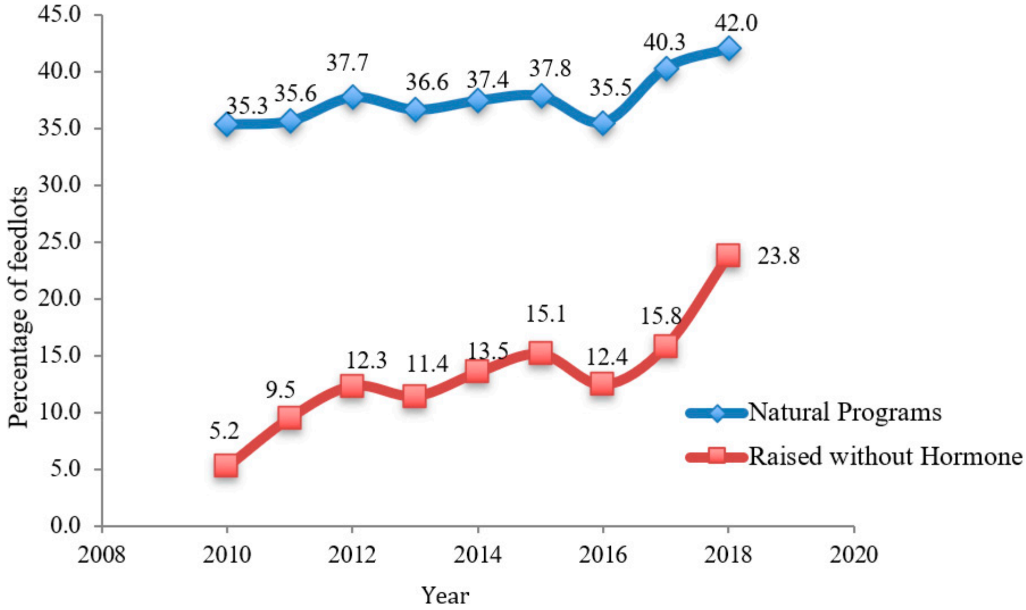

Figure 3. Percentage of feedlots that enrolled in "raised without hormone" or in one or more "natural" programs in Texas, US. Source: Modified from Odde et al. [61].

5. PETs and the Environment

The use of PETs leads to improved production efficiencies [37,48,52]. However, assessments of the effects of PETs on the environmental footprint, including GHG emissions, land use and land use change, water and energy use, and impacts on biodiversity, water quality, and other ecosystem services are limited. Moreover, available studies have focused primarily on production systems in Canada and the US (Table 2).

5.1. Greenhouse Gas Emissions and Resource Use

The environmental impact of GHG emissions including methane (CH_4), nitrous oxide (N_2O), and carbon dioxide (CO_2) associated with beef production is arguably one of the environmental concerns of consumers [57,68]. A consumer survey in Canada revealed that environmental and animal welfare concerns were the primary reasons that 6.4 million Canadians either restricted or eliminated meat from their diet, with the majority of those respondents aged 18 to 36 and possessing graduate degrees [69].

As a consequence of these environmental concerns, several studies have been conducted in the past decade to assess the benefits of PETs on the environmental footprint of beef. In these studies, the beneficial effects of PETs on greenhouse gases and resources were mostly seen on an intensity basis (i.e., unit of measure/kg of beef). A study conducted in the US [70] examined the impact of PETs on CH_4 emissions of 160 Angus beef cattle (n = 40 head/treatment) during the last 10 days of four feeding periods (86, 110, 114, and 128 days, based on body weights). The animals were divided into four treatments during finishing: (i) control (no additives) and tylosin with either (ii) ionophores (MON), (iii) implants (TBA + E) + MON, or iv) TBA + E + MON + βAA (ZC). Although CH_4 emissions did not differ between the control and TBA + E + MON treatments (0.73 vs. 0.71 g CH_4/ kg of beef), MON-only and the TBA + E + MON + ZC, decreased the intensity of CH_4 emission by 9.6% (0.66 g CH_4/ kg of beef) and 16.4% (0.61 g CH_4/ kg of beef), respectively [70]. The lack of effect of the TBA + E + MON treatment on CH_4 emissions is surprising, as the average daily gain and feed efficiency of this treatment was improved relative to the control. An increase in DMI due to the growth implants may have offset the decreased DMI promoted by the ionophores, resulting in no effect on the intensity of CH_4 emissions.

Table 2. Summary of studies measuring the environmental impacts of productivity-enhancing technologies (PET) used in beef production.

Reference	Summary of Trial Design				Environmental Indices [e,f]					Country
	Methodology [a]	Production Stage [b]	Treatment [c]	Days on Feed	CO_2eq	Land	Water	Energy	NH_3 /Manure Excretion	
Basarab et al. [73]	LCA	Backgrounding and finishing phases	IMP or control	Backgrounding: 312 days. Finishing: 146 to 207 days.	5.8% ↓	7.8% ↓	NR	NR	NR	Canada
Capper [72]	LCA	Backgrounding and finishing phases	βAA + IMP + MGA + ION (“conventional”); and no additives (“grass-fed” or “natural” animals).	Backgrounding: 123 to 159 days. Finishing: 110 to 313 days.	14.8–40.3% ↓	18.3–44.7% ↓	17.9–75.2% ↓	14.9–28.6% ↓	17.9–50.5% ↓ N and 20.7–51.4% ↓ P excretions	US
Capper and Hayes [74]	LCA	Backgrounding and finishing phases	βAA + IMP + ION + MGA; or control.	Backgrounding: 148 to 159 days. Finishing: 116 to 209 days.	8.9% ↓	9.1% ↓	4.0%↓	7.1% ↓	8.9% and 9.6%, ↓ N and P excretions, respectively.	US
Cooprider et al. [71]	Animal trial	Finishing phase	βAA + IMP + ION; or control.	146 to 188 days.	31.4% ↓ non-CO_2 emissions	NR	NR	NR	NR	US
Stackhouse et al. [75]	LCA	Backgrounding and finishing phases	IMP + ION only; βAA + IMP + ION; or control.	Backgrounding: 182 days. Finishing: 121 to 212 days.	6.6–8.0% ↓	NR	NR	NR	7.7–13.5% ↓ NH_3 emissions.	US
Stackhouse-Lawson et al. [70]	Animal trial	Finishing phase	ION only; IMP + ION only; βAA + IMP + ION; or control	107 days.	9.6–16.4% ↓CH_4 emissions	NR	NR	NR	30% ↓ NH_3 emissions	US
Webb [76]	Animal trial and LCA	Cow–calf, backgrounding, and finishing phases	ION only; IMP + ION only; βAA + IMP + ION; or control.	Backgrounding: 91 days, Finishing: 152 to 183 days	1.1–7.7% ↓	NR	1.0–5.8% ↓	1.1–5.5% ↓	0.7–5.1% ↓ reactive N	US

[a] Type of study conducted: LCA = Life cycle assessment, with PETs administered during backgrounding and finishing phases only, except Webb [76], who included implanted pre-weaned calves during the cow–calf phase; Animal trial = a study that used steers at the finishing phase. [b] Assumes a production system comprised of three distinct phases: cow–calf, backgrounding, and finishing. Grain-based diet during finishing phase except where indicated. [c] IMP = Implants (trenbolone acetate, estradiol, zearalenone); MGA= melengestrol acetate; ION = Ionophores (Monensin); βAA = Beta-adrenergic agonist (zilpaterol chloride and ractopamine chloride). [d] ADG = average daily gain; G:F = gain:feed. In Stackhouse et al. [75] and Webb [76], linear growth was assumed during the backgrounding phase; and during the finishing phase, ADG was adjusted when days on feed were extended as a consequence of lower feed quality and availability, which were assumed to limit growth. [e] Where ↓= decrease, ↑ = increase, and NR= not recorded; In all studies, the production indices and environmental parameters for all PET treatments were compared with control (no additives); however, in Capper [72], “conventional” animals (administered PETs) were compared with “natural” or “grass-fed” animals (no PETs administered for either). [f] Environmental indices were expressed on an intensity basis (per kg of beef); CO_2eq = carbon dioxide equivalent; CH_4 = methane; NH_3 = ammonia; N = Nitrogen; and P = Phosphorus. [g] The total number of cattle considered under “grass-fed” was 12,510,000 and for “natural” was 8,257,000 animals. [h] The total number of cattle in the production system without PETs was 3,651,000 animals.

Cooprider et al. [71] also assessed the environmental impact of PETs in 104 Angus beef assigned to (n = 52 head treatment/treatment) (i) control and (ii) PET-treated cattle (TBA plus E administered with tylosin, MON, and RC). Cattle administered PETs grew faster with a 22% decrease in days on feed (146 vs. 188 days), and a 24% reduction in DMI (1112 vs. 1462 kg/steer) compared to controls [71]. Although there was no difference in daily non-CO_2 (CH_4 and N_2O) emissions from PET-treated animals compared to controls over a measurement period of five days (300.3 vs. 286.6 g non-CO_2/day), emissions decreased by 31.4% throughout the finishing phase when adjusted for intake (30.2 vs. 33.5 g non-CO_2/kg DMI), primarily due to a reduction in DMI and days on feed prior to marketing [71].

Using a deterministic environmental impact model (EIM) with a national database, Capper [72] simulated different production systems in the US, where beef cattle were either managed in "grass-fed", "natural", or "conventional" systems while producing the same quantity of beef in a year. The system boundaries in the model (i.e., beef population, animal system, and transport system) were the same, but the cropping system varied, because the diets for the "natural" and "conventional" beef cattle (i.e., containing grain) differed from "grass-fed" cattle. "Natural" and "grass-fed" cattle were also raised without PETs at the cow–calf, backgrounding, and finishing stages, whereas PETs (TBA, E, MGA, and MON) were used throughout the "conventional" beef cattle production cycle, except during the pre-weaning phase with ZC or RC also administered during the finishing phase. Cattle were harvested at 15 and 22 months in the "natural" and "grass-fed" systems, respectively. Cattle in the "conventional" system reached slaughter weight at 14 months. This simulation showed that to produce the same amount of beef, 17.2% and 77.5% more animals were required for the "natural" (~8.3 million) and "grass-fed" (~12.5 million) systems as compared to the "conventional" system [72]. Consequently, to sustain the quantity of beef consumed, feed, land, and water use, expressed on an intensity basis, increased by 23.5% (67.3 vs. 54.5 kg/kg of beef), 22.4% (66.8 vs. 54.6 m^2/kg of beef), and 17.9% (572.5 vs. 485.7 L/kg of beef), respectively, for the "natural" as compared to the "conventional" production system [72]. Feed requirements (51.7 kg increase, 94.9%), land use (44.1 m^2 increase, 80.3%), and water use (1471.5 L increase, 302.8%) per kg of beef were increased when the production system was shifted towards "grass-fed" beef raised without PETs [72]. Furthermore, raising cattle without PETs to produce "natural" or "grass-fed" beef increased the carbon footprint intensity by 17.4% (18.8 vs. 15.9 CO^2eq/kg of beef) or 67.5% (26.8 vs. 15.9 CO^2eq/kg of beef), respectively [72].

Using the same national database and system boundaries, Capper and Hayes [74] also modeled the US production system to determine the effects of removing growth hormones, ionophores, and βAA on productivity (growth rate and slaughter weight) of both beef and calf-fed dairy (moved directly from the cow–calf to the finishing phase after weaning) as well as yearling-fed cattle that entered the feed yard after the backgrounding phase [74]. Removal of PETs resulted in the need for approximately 11.7% (385,000) more cattle to produce the same yearly quantity (454 million kg) of beef [74]. Consequently, the intensity of feed, land, and water required to sustain beef production also increased by 10.5% (65.3 vs. 59.0 kg/kg of beef), 10.1% (64.1 vs. 58.2 m2/kg of beef), and 4.2% (1099.8 vs. 1055.4 L/kg of beef), respectively, resulting in a 9.8% increase in the carbon footprint intensity [74].

Stackhouse et al. [75] used the integrated farm system model (IFSM) to estimate the carbon footprint of typical beef production systems in California. This simulation used a cradle-to-farm gate approach with system boundaries including beef (cow–calf, backgrounding, and finishing phases) and feed production, and the use of other resources (e.g., fertilizer, fuel, electricity, machinery). The treatments included (i) control (no additives), (ii) TBA + E + MON, or (iii) TBA + E + MON + ZC. All treatments were administered from backgrounding through finishing stages except ZC, which was only administered at the finishing stage [75]. Cattle were fed for 365, 182, and 121 days, depending on the stage of production. Also included in this simulation were calf-fed cattle, which received a finishing diet for 212 days. The authors showed that the removal of TBA + E + MON or TBA + E + MON + ZC from beef production resulted in a 6.6% (24.2 vs. 22.6 CO2eq/kg of beef) or 9.1% (24.2 vs. 22.0 CO2eq/kg of beef) increase in the carbon footprint intensity, respectively [75]. The effects of PETs on the carbon footprint were mainly due to their impact on productivity, as the numbers of days on feed were the same. The authors also reported a 6.2% increase in the carbon footprint intensity (22.6 vs. 21.2 CO2eq/kg of beef) as a result of removing TBA + E + MON from calves that were placed directly on the finishing diet after weaning. The average values of the carbon footprint with or without the backgrounding stage for the PET treatments (22.3 or 21.2 CO2eq/kg of beef [75]) indicated that most of the GHG emissions arose from the cow–calf stage, a point in the production chain where cattle are not commonly administered PETs.A similar analysis of the environmental impacts of beef cattle in the US Northern plains was simulated using IFSM, with (i) control, (ii) MON only, (iii) TBA + E + Z + MON, or iv) TBA + E + Z + MON + RC as treatments [76]. Trenbolone acetate, E, and Z implants were administered at the cow–calf, backgrounding, and finishing phases. Monensin and RC were administered during the finishing phase. The cow–calf operation included 270 cows with calves weaned after six months, followed by backgrounding and finishing. The backgrounding and finishing phases were assumed to consist of 4000 (91 days on feed) and 5000 cattle (152 or 183 days depending on the treatments), respectively. Compared to the control, the authors showed that the removal of MON-only, TBA + E + Z + MON, or the combination of TBA + E + Z + MON + RC increased water-use/kg of beef by 1.0% (31 L increase), 6.1% (173 L increase), or 4.6% (131 L increase), respectively [76]. Compared with the control (43.3 MJ), the energy used to produce an equivalent amount of beef also increased by 0.5%, 5.6%, and 3.6%, by removing MON alone (0.2 MJ increase), TBA + E + Z + MON (2.3 MJ increase), and TBA + E + Z + MON + RC (1.5 MJ increase), respectively. Therefore, the carbon footprint for the same quantity of beef increased when MON only (0.2 CO_2eq increase; 1.1%), TBA + E + Z + MON (1.4 CO_2eq increase; 7.7%), or TBA + E + Z + MON + RC (1.1 CO_2eq increase 6.1%), were removed for the beef production system. In this study, the effect of PETs was confounded by a difference in the number of days on feed at the finishing phase, which was the same for control and TBA + E + Z + MON treatments (152 days, a month less than the other treatments) as cattle were slaughtered on the basis of a standard level of backfat thickness (~1.53 cm 12th rib). This reduction of days on feed explains the greater decline in the environmental footprint of implanted cattle fed MON relative to controls.

Basarab et al. [73] also used simulations to examine the impact of removing PET from Canadian beef production by modeling a calving herd (~350 beef cows) over two production cycles. This simulation used a customized whole-farm GHG emissions model within the calf-fed (slaughtered age 11 to 14 months) and yearling-fed (19 to 23 months) production systems. The system boundaries were similar to those described by Stackhouse et al. [75], and within each production system, the number of days on feed was kept constant between implanted and control animals [73]. The results indicated that the use of growth hormones increased the total amount of feed required by 0.8% (9 t increase) and total land by 0.4% (1.2 ha increase) for calf-fed animals. Total feed and land also increased by 1.5% (22 t increase) and 1.0% (3.9 ha increase) for implanted yearling-fed animals, respectively [73]. However, without hormonal implants, the land base required to produce a kg of beef from the calf-fed and yearling fed feeding systems increased by 8.5% (0.9720 vs. 1.0546 t/kg of beef) and 8.4% (0.9420 vs. 1.0207 t/kg of beef), respectively [73]. Although the total feed demand of implanted animals increased, they required less land to produce a comparable quantity of beef due to improved feed efficiency. Implants also lowered the carbon footprint intensity of these beef production systems by 5.8% (21.81 vs. 20.54 kg CO_2eq/kg beef [73]). These results are comparable to a meta-analysis in which implanted cattle exhibited increased feed intake and weight gain compared to control cattle [34].

All studies reported in Table 2 demonstrated a positive environmental impact associated with the use of PETs. Variations in the magnitude of response may be attributed to differences in methodology (LCA analysis vs. animal trials) and management practices including type, timing, and duration of PET use, number of days on feed, and final carcass weight. However, these studies are limited to the US and Canada, and more studies are needed globally to understand impact of PETs across a range of management practices on energy, water, and land use efficiency.

5.2. Environmental Contamination

Globally, there are also concerns that excretion of PETs and their metabolites in beef cattle manure (faces and urine) may contaminate water bodies and potentially disrupt endocrine and reproductive functions in terrestrial, amphibians, and aquatic animals [77]. These growth promotants may be transported via leakage from storage structures and run-off from feed yards and manure-amended soil [78,79] and in airborne particulate matter [80]. In the US, RC has been detected in airborne particulate matter (4700 ng/g) in the feed yard and also in water bodies (271 ng/L) near the feed yard [81]. The transport of RC in water bodies and the feed yard is possible, as a recent study by Challis et al. [82] in Canada confirmed that by feeding RC to feedlot cattle for 42 days, RC was still detected in the pen floor feces during (13 days; 3600 ng/g) and post feeding (37 days; 681 ng/g) such that run-off manure from pen floors and pasture contained RC at concentrations of 6300 and 2100 ng/L, respectively. The authors also showed that catch basins near commercial feedlots in Lethbridge, Canada, can contain RC at concentrations of 4000 to 27,000 ng/L in water and 234 to 1506 ng/g in sediment [82]. Groundwater adjacent to cattle operations in Nebraska was also found to contain MON at concentrations ranging from 20 to 2080 ng/L, and the metabolites of steroidal hormones (i.e., estrone, testosterone, 4-androstenedione, and androsterone) ranging from 40 to 390 ng/L, and [83]. As these steroidal hormones are also occurring naturally in cattle, their excretion (e.g., estrogens) in manure depends on gender, age, and reproductive status [84].

Synthetic hormones have been shown to affect the reproductive function of organisms in a laboratory setting. Compared to quail that did not receive TBA, hens [85] or their male embryos [86] exposed to 20 or 50 ppm TBA showed a reduction in the number of maturing follicles and egg production as well as delayed onset of puberty. Further, male fish exposed to estrogen at concentrations higher than 72 ng/L for 21 days were less aggressive than their unexposed counterparts [87]. In addition, frog embryos exposed to either TBA (500 ng/L) or MGA (100 ng/L) alone or in combination exhibited decreased larval growth and impaired development, with no impact on mortality [88].

Two main Canadian rivers situated close to beef cattle feedlots in the province of Alberta (Bow and Oldman rivers) were found to contain hormones, including the synthetic hormone zearalenone at concentrations of 5.16 ng/L, and the concentrations of the zearalenone were associated with estrogenic (feminizing) activities in male fish [89]. However, the zearalenone concentrations in the Bow and Oldman rivers were 9- to 193-fold below the threshold necessary to cause adverse impacts on aquatic species (i.e., 50 to 1000 ng/L [90–92]). It is likely that the shifted sex effect reported by Jeffries et al. [89] in male fish collected from these rivers could have been significantly influenced by hormones released from other sources, including crop production and municipal wastewater treatment plants [93]. For example, at detectable concentrations, contaminants from *Fusarium*-infected grains such as corn, barley, and other small grain crops can contribute to zearalenone concentrations in manure and surface run off [94,95]. Globally, municipal wastewater treatment is arguably the principal source of hormones that are released into the environment, as beef-producing countries that do not use PETs have also reported effects of hormones on aquatic biodiversity [96,97]. Therefore, the implications of removing PETs from beef operations without addressing other point and non-point sources is unknown.

Synthetic hormones are rapidly metabolized in the gastrointestinal tract of animals [98], and their metabolites (e.g., 17α-trenbolone and 17β-trenbolone) are also quickly degraded in manure, contributing to their short half-lives (i.e., 4 to 50 h and 5 to 15 h, respectively) [99]. However, endogenous hormones and their metabolites (e.g., testosterone, 4-androstenedione, 17β-estradiol, estrone, progesterone, and 17α-hydroxyprogesterone) have been detected after 100 days in manure from cattle that did and did not receive TBA, E, Z, or MGA in the US [99]. Similarly, in Canada, due to the fast degradation rate of TBA, its metabolites (17α-trenbolone and 17β-trenbolone), and MGA, these PETs were below the detection limit in manure of treated cattle, but the βAA and RC persisted in manure from the pen floor due to its slow rate of degradation (half-lives of 18 to 49 days [82]). Researchers have shown that composting and stockpiling cattle manure can reduce endogenous hormones in manure. Using composting and stockpiling, a study in the US reported no significant difference in the concentrations of TBA, E, Z, and MGA (average, 19.0 ng/g of dry weight) in manure from cattle that did or did not receive these additives [94]. This group also showed that composting (12.3 ng/g of dry weight) is more effective than stockpiling (25.7 ng/g of dry weight) at reducing hormone concentration in surface water run-off from the feedlot. Composting has also been proven in Canada to dissipate the antibiotic, tylosin, in excreted manure of beef cattle by 85% [100]. This suggests that composting as a means of handling cattle manure could also potentially reduce other PET residues in manure, including RC, which can persist in the pen floor for up to 39 days [82]. Thus, the effect of compositing on RC residue in manure requires further exploration.

Productivity-enhancing technologies have also been shown to decrease the excretion of nutrients (e.g., nitrogen (N), phosphorus (P), and ammonia (NH_3)) that can contribute to the eutrophication of aquatic ecosystems in various habitats [101]. Capper and Hayes [74] showed that without PETs, manure excretion increased by 10%, as more cattle were required to produce an equivalent amount of beef in the US (454 million kg of beef). As a result, N and P excretion also increased by 9.7% and 10.6%, respectively, [74]. Similarly, in a simulated study, cattle raised without PETs in the US such as "natural" or "grass-fed" cattle had 21.7% or 102.0% greater N and or 26.1% or 105.9% greater P excretion in manure, respectively, relative to those raised in a "conventional" system [72]. Stackhouse-Lawson et al. [70] also reported that compared to the control treatment, manure NH_3 emissions increased for implanted and cattle that received MON only, but decreased in manure from cattle administered MON with ZC during the last 20 days of finishing. Furthermore, in a LCA study, Stackhouse et al. [75] reported that compared to "natural" systems, the total NH_3 emissions/kg of beef from the feedlot, manure storage, field applied manure, and direct deposits of manure on pasture and rangeland by grazing cattle was reduced by 7.7% or 13.5% if cattle were administered TBA, E, and MON or for those that received the same treatment plus ZC, respectively. Similarly, via an LCA, Webb [76] also estimated reactive N losses (NH_3 emissions, nitrate leaching and runoff, and nitrous oxides) from housing facilities, stored manure, and direct and applied manure on pasture. Relative to the control treatment, reactive N/kg of beef produced was not affected by MON-only, but decreased in manure from implanted cattle + MON and in manure from implanted cattle that received MON + RC by 5.1% and 0.7%, respectively. Though the dietary crude protein level was not reported in the studies by Stackhouse et al. [75] and Webb [76], it can influence N excretion with greater excretion as dietary protein increases, and this may have partly contributed to the different effects of the PET treatments on N excretion. Nonetheless, there was an additive effect with βAA and implants in reducing N release to the environment in both studies. The reported decrease in environmental N components with βAA may be attributed to their capacity to shift dietary N to muscle formation [102], while the implants ensured N retention and improved efficiency by decreasing protein degradation or increasing fat deposition [30].

6. PET, Food Safety, and Animal Welfare

Concerns regarding the development and spread of antimicrobial resistance due to the use of antibiotics for growth promotion in animals has recently led to the ban of in-feed antibiotics such as tetracycline and tylosin for growth promotion in many countries including Canada (Table 1 [103]). These antibiotics are used in treating infectious disease in animals as well as humans, and therefore there are concerns that this practice may compromise the therapeutic effectiveness of antimicrobial drugs in human medicine [104]. The Global Roundtable for Sustainable Beef (GRSB), which represents beef producers, veterinarians, scientists, retailers, and other value chain partners in over 20 countries, recommended that with the exception of ionophores, antimicrobials should not be used for feed efficiency [105]. Ionophores are not currently used for therapeutic purposes in humans [104]. Wong [106] argued that ionophores such as MON are technically antibiotics and should also be banned. However, implementation of this recommendation is at the discretion of local and national legislative and regulatory authorities.

Furthermore, approval of PETs for use requires toxicology testing to determine maximum residue limits (MRLs) in beef for human consumption. While others have adopted the guidelines of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), some countries have developed their own guidelines [107–109]. Due to differences among guidelines, the MRLs established for PETs in beef and beef products may be low or non-existent in some countries. Independent institutions including JECFA and government institutions from several countries including Canada, Australia, and the US do not analyze the offal (i.e., abomasum, omasum, small intestine, and reticulum) for βAA. Consequently, there are no established MRLs for this PET in these tissues. In a recent US study by Davis et al. [110], RC concentrations were higher in offal (13 to 105 ppb) and in small intestinal digesta (20 ppb) from beef cattle than the limits recommend in the muscle tissue by most countries (i.e., 10 to 30 ppb). The lack of established MRLs means that beef products such as edible offal may exceed recommended allowable limits, as was the finding of Davis et al. [110]. There are limited studies on the effects of RC and ZC on human health, but preliminary data reviewed by authorities at the European Food Safety Authority (EFSA) suggested that a single dose ($\geq$0.76 µg/kg body weight) of these βAA may cause transient cardiovascular disease and bronchodilation, posing a risk to asthmatic patients [111]. However, residue levels in muscle, liver, and kidney were well below the MRLs established by regulatory agencies in Canada [112], Australia [113], and the US [114].

There are also animal welfare concerns due to the use of diethylstilbestrol (a hormone) and clenbuterol (a βAA) as a consequence of their endocrine disrupting properties [115,116], dilation of the trachea [117], and disruption of metabolism [118]. As result of concerns over these responses, the use of these additives in beef production has been discontinued. Nevertheless, worldwide, there are animal welfare concerns regarding currently used βAA products such as ZC. More recently in the US, Neary et al. [119], hypothesized that ZC (8.3 mg/kg on feed DM basis for 21 days) increased the risk of cattle developing heart disease. In that same year of their experiment, the use of this product also was proposed to contribute to the development of lameness and increase the mortality of cattle during the finishing phase [120]. In 2013 and 2014, some of the largest meat processing plants such as Tyson Foods and Cargill in both the US and Canada suspended the purchase of cattle fed this product. Subsequently, Merck Animal Health also removed this product from the market until such a time that additional data can be generated to evaluate product safety [121,122].

To address concerns relating to ZC use, scientists from EFSA reviewed 12 studies between 2012 and 2016 (excluding [119]) to examine the animal health and welfare of more than 200 cattle and concluded that ZC was not responsible for death and lameness in beef cattle [111]. Although a study by Neary et al. [119] (n = 11) suggested that ZC may compromise cardiac function, it is possible that other respiratory diseases were responsible, possibly making the link between cardiac injury and ZC coincidental [123–125]. A follow-up US study using 30 Angus steers showed no evidence of myocardial injuries or an increase in heart rate associated with ZC (8.3 mg/kg on feed DM basis) and RC (300 mg/d) after 23 days of treatment [126]. Similarly, after feeding RC to finishing cattle at 400 mg/d, Hagenmaier et al. [127] did not report an increase in heart rate. In addition to concerns regarding physiological responses to PETs, public perception suggests that their use leads to increased stocking density and compromised animal welfare. Decisions regarding stocking density are based on adequate bunk space in conventional systems and forage availability in pasture-based systems, and in either case are not dictated by PET use. Thus, with the current recommended dosages and administration guidelines, these PETs have not been reported to have adverse effects on consumer health or animal welfare.

7. Future Directions

The use of PETs has improved the efficiency of beef production for more than 50 years in Canada, Australia, and the US, while reducing the cost of production and offering affordable beef for both domestic and international markets. However, consumer concerns about the potential negative impact of PETs on wildlife habitats, animal welfare, and food safety have increased. Science-based evidence gathered herein indicates that the use of PETs in beef production can mitigate GHG and NH_3 emissions, while increasing biodiversity by reducing land, water, and energy use, relative to urban and other agricultural practices. However, given the existing misconceptions regarding the use of PETs, it is difficult to convey the benefits of use to consumers in a soundbite of information, such as a label claim. Recently, a βAA product (Experior-lubabegron) has been approved both in the US [128] and Canada [129] with an NH_3 emissions reduction feed label claim. Therefore, the potential exists for this information to be included in food label claims in the future. This review highlights the need to examine and contrast the environmental vs. consumer trade-offs of PETs in countries that have traditionally used these technologies, as well as in those that are considering their adoption.

In 2019, the US dollar value of beef exported by these PET-beef producing countries including Australia (7.6 billion), US (6.9 billion), Brazil (6.5 billion), Argentina (3.1 billion), New Zealand (2.4 billion), and Canada (2.18 billion) corresponded to 55.5% of global exports (51.7 billion [130]). These beef-exporting countries could potentially garner higher premiums from niche markets based on consumer demand for PET-free beef. However, an increase in the quantity of PET-free beef may depend on trade agreements between countries as well as domestic demand for dietary protein. In the recent Comprehensive Economic and Trade Agreement between Canada and Europe (imports only PET-free beef into the EU countries), the quota of PET-free beef exported from Canada to the EU has increased and is duty-free [131]. As the EU is among the highest-priced and largest beef markets in the world, it was estimated that production of PET-free beef for export into Europe could contribute about CAD$ 600 million annually to the Canadian economy [132]. However, there are still some non-tariff trade barriers, which makes it difficult for beef producers in Canada to export to the EU [133]. Whether this premium is sufficient for producers to eliminate PETs may depend on the profit they accrue [61]. Therefore, it is important for countries that restrict the use of PETs to cease using them as non-tariff trade barriers, as their use could result in a reduction in the environmental footprint of beef productions.

Conversely, with the African Swine Fever outbreak in China and the subsequent COVID-19 pandemic, the government of China removed its ban on the import of hormone-treated beef and has recently signed a trade agreement with the US. This agreement allows the import of beef from hormonal implanted cattle into the country while maintaining its zero-tolerance for βAA [134]. While this trade agreement will contribute to meeting the protein demands of China, it also provides opportunities for US producers to supply beef at a reduced cost to the Asian market. The EU and China examples demonstrate that the demand and supply of PET-free beef is not constant. It may be influenced by factors within trade agreements that make this practice profitable as well as other drivers (e.g., zoonotic, epidemiologic global crises, increased consumption of meat alternatives) that can cause a sudden shift in demand.

8. Conclusions

Productivity-enhancing technologies have been shown to improve production efficiency and therefore play a role in contributing to the global sustainability of beef production. However, the effects of PETs on addressing consumer concerns regarding the environmental footprint of beef production are offset by consumer perceptions about the impact of PET on the environment, animal welfare, and food safety. The beef industry can realize premiums from domestic and international demand by adopting management practices that do not use PETs to raise cattle and sustain beef production. Nevertheless, because PETs reduce the cost of production, the potential for economic viability will depend on the magnitude of the premiums realized. For consumers, withdrawal of PETs can have negative implications for the environment and increase the retail price of beef, potentially impacting low-income consumers who would benefit the most from the favorable nutrient profile of beef. Globally, scientific data regarding the effects of removing PETs on environmental inputs and outputs are limited to Canada and the US. Furthermore, there is an increasing effort to identify feed additives, which increase production and decrease the environmental impacts of beef production. As global data on hormones, ionophores, βAA, and other non-conventional feed additives (e.g., plant extracts, probiotics, and immune stimulators) become available through further research, a meta-analysis to determine individual and combined impact on land, water, and energy use, as well as biodiversity, is warranted. Such analysis is critical to provide stakeholders including consumers, governments, and producers with comprehensive science-based evidence regarding the environmental impacts of traditional and emerging PETs.

Author Contributions: Conceptualization: I.A.A., M.R.C.C., T.A.M., and K.H.O.; writing—original draft preparation: I.A.A.; writing—review and editing: I.A.A., M.R.C.C., T.A.M., and K.H.O.; funding acquisition: T.A.M. and K.H.O. All authors have read and agreed to the published version of the manuscript.

Funding: The study was funded by the Beef Cattle Research Council and Agriculture and Agri-Food Canada through the Sustainable Beef and Forage Science Cluster (ENV.15.17; 2018–23).

Data Availability Statement: Not applicable.

Acknowledgments: Authors are thankful to the anonymous reviewers whose critiques and comments greatly improved the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. United Nations. Department of Economic and Social Affairs. Population Division. World Population Prospects. 2019. Available online: https://population.un.org/wpp/Graphs/Probabilistic/POP/TOT/900 (accessed on 10 January 2020).
2. Adesogan, A.T.; Havelaar, A.H.; McKune, S.L.; Eilittä, M.; Dahl, G.E. Animal source foods: Sustainability problem or malnutrition and sustainability solution? Perspective matters. *Glob. Food Sec.* **2020**, *25*. [CrossRef]
3. Lonnie, M.; Hooker, E.; Brunstrom, J.M.; Corfe, B.M.; Green, M.A.; Watson, A.W.; Williams, E.A.; Stevenson, E.J.; Penson, S.; Johnstone, A.M. Protein for life: Review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. *Nutrients* **2018**, *10*, 360. [CrossRef] [PubMed]
4. Van Zanten, H.H.E.; Meerburg, B.G.; Bikker, P.; Herrero, M.; De Boer, I.J.M. Opinion paper: The role of livestock in a sustainable diet: A land-use perspective. *Animal* **2016**, *10*, 547–549. [CrossRef] [PubMed]
5. Food and Agriculture Organization (FAO). *Dietary Protein Quality Evaluation in Human Nutrition*; Report of an FAO Expert Consultation; FAO: Rome, Italy, 2013.
6. Gorissen, S.H.M.; Witard, O.C. Characterising the muscle anabolic potential of dairy, meat and plant-based protein sources in older adults. *Proc. Nutr. Soc.* **2018**, *77*, 20–31. [CrossRef]
7. Van Vliet, S.; Burd, N.A.; van Loon, L.J.C. The skeletal muscle anabolic response to plant- versus animal-based protein consumption. *J. Nutr.* **2015**, *145*, 1981–1991. [CrossRef]
8. Obersby, D.; Chappell, D.C.; Dunnett, A.; Tsiami, A.A. Plasma total homocysteine status of vegetarians compared with omnivores: A systematic review and meta-Analysis. *Br. J. Nutr.* **2013**, *109*, 785–794. [CrossRef]
9. Magkos, F.; Tetens, I.; Bügel, S.G.; Felby, C.; Schacht, S.R.; Hill, J.O.; Ravussin, E.; Astrup, A. A Perspective on the transition to plant-based diets: A diet change may attenuate climate change, but can it also attenuate obesity and chronic disease risk? *Adv. Nutr.* **2020**, *11*, 1–9. [CrossRef]
10. Haider, L.M.; Schwingshackl, L.; Hoffmann, G.; Ekmekcioglu, C. The effect of vegetarian diets on iron status in adults: A systematic review and meta-analysis. *Crit. Rev. Food Sci. Nutr.* **2018**, *58*, 1359–1374. [CrossRef]
11. Phillips, S.M. Nutrient-rich meat proteins in offsetting age-related muscle loss. *Meat Sci.* **2012**, *92*, 174–178. [CrossRef]

12. Tang, J.E.; Moore, D.R.; Kujbida, G.W.; Tarnopolsky, M.A.; Phillips, S.M. Ingestion of whey hydrolysate, casein, or soy protein isolate: Effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. *J. Appl. Physiol.* **2009**, *107*, 987–992. [CrossRef]
13. Wilkinson, S.B.; Tarnopolsky, M.A.; Macdonald, M.J.; Macdonald, J.R.; Armstrong, D.; Phillips, S.M. Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. *Am. J. Clin. Nutr.* **2007**, *85*, 1031–1040. [CrossRef]
14. Herrero, M.; Havlík, P.; Valin, H.; Notenbaert, A.; Rufino, M.C.; Thornton, P.K.; Blümmel, M.; Weiss, F.; Grace, D.; Obersteiner, M. Biomass use, production, feed efficiencies, and greenhouse gas emissions from global livestock systems. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 20888–20893. [CrossRef]
15. Gerber, P.J.; Steinfeld, H.; Henderson, B.; Mottet, A.; Opio, C.; Dijkman, J.; Falcucci, A.; Tempio, G. *Tackling Climate Change Through Livestock: A Global Assessment of Emissions and Mitigation Opportunities*; FAO: Rome, Italy, 2013.
16. Poore, J.; Nemecek, T. Reducing food's environmental impacts through producers and consumers. *Science* **2018**, *360*, 987–992. [CrossRef]
17. Eshel, G.; Shepon, A.; Makov, T.; Milo, R. Land, irrigation water, greenhouse gas, and reactive nitrogen burdens of meat, eggs, and dairy production in the United States. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 11996–12001. [CrossRef]
18. Lobato, J.F.P.; Freitas, A.K.; Devincenzi, T.; Cardoso, L.L.; Tarouco, J.U.; Vieira, R.M.; Dillenburg, D.R.; Castro, I. Brazilian beef produced on pastures: Sustainable and healthy. *Meat Sci.* **2014**, *98*, 336–345. [CrossRef]
19. Wiedemann, S.G.; Henry, B.K.; McGahan, E.J.; Grant, T.; Murphy, C.M.; Niethe, G. Resource use and greenhouse gas intensity of Australian beef production: 1981–2010. *Agric. Syst.* **2015**, *133*, 109–118. [CrossRef]
20. Capper, J.L. The environmental impact of beef production in the United States: 1977 compared with 2007. *J. Anim. Sci.* **2011**, *89*, 4249–4261. [CrossRef]
21. Legesse, G.; Beauchemin, K.A.; Ominski, K.H.; McGeough, E.J.; Kroebel, R.; MacDonald, D.; Little, S.M.; McAllister, T.A. Greenhouse gas emissions of Canadian beef production in 1981 as compared with 2011. *Anim. Prod. Sci.* **2016**, *56*, 153–168. [CrossRef]
22. Legesse, G.; Cordeiro, M.R.C.; Ominski, K.H.; Beauchemin, K.A.; Kroebel, R.; McGeough, E.J.; Pogue, S.; McAllister, T.A. Water use intensity of Canadian beef production in 1981 as compared to 2011. *Sci. Total Environ.* **2018**, *619–620*, 1030–1039. [CrossRef]
23. Strydom, P.E. Performance-enhancing technologies of beef production. *Anim. Front.* **2016**, *6*, 22–30. [CrossRef]
24. Godfray, H.C.J.; Aveyard, P.; Garnett, T.; Hall, J.W.; Key, T.J.; Lorimer, J.; Pierrehumbert, R.T.; Scarborough, P.; Springmann, M.; Jebb, S.A. Meat consumption, health, and the environment. *Science* **2018**, *361*. [CrossRef] [PubMed]
25. Jeong, S.H.; Kang, D.; Lim, M.W.; Kang, C.S.; Sung, H.J. Risk assessment of growth hormones and antimicrobial residues in meat. *Toxicol. Res.* **2010**, *26*, 301–313. [CrossRef]
26. Nachman, K.E.; Smith, T.J. Hormone use in food animal production: Assessing potential dietary exposures and breast cancer risk. *Curr. Environ. Health Rep.* **2015**, *2*, 1–14. [CrossRef] [PubMed]
27. Nielsen Global Health and Ingredient-Sentiment Survey. What's in Our Food and on Our Mind? Ingredient and Dining-Out Trends around the World. 2016. Available online: https://nutrimento.pt/activeapp/wp-content/uploads/2016/09/global-ingredient-and-out-of-home-dining-trends-aug-2016.pdf (accessed on 25 March 2020).
28. Johnson, B.J.; Beckett, J. Application of Growth Enhancing Compounds in Modern Beef Production Executive Summary. Available online: https://meatscience.org/docs/default-source/publications-resources/white-papers/application-of-growth-enhancing-compounds-in-modern-beef-production-2015-final.pdf?sfvrsn=a9180b3_2 (accessed on 25 March 2020).
29. Stewart, L. *Implanting Beef Cattle*; The University of Georgia Cooperative Extension: Athens, GA, USA, 2013; Available online: http://extension.uga.edu/publications/detail.html?number=B1302&title=Implanting%20Beef%20Cattle (accessed on 5 March 2020).
30. Lone, K.P. Natural sex steroids and their xenobiotic analogs in animal production: Growth, carcass quality, pharmacokinetics, metabolism, mode of action, residues, methods, and epidemiology. *Crit. Rev. Food Sci. Nutr.* **1997**, *37*, 93–209. [CrossRef]
31. McDonald, P.; Edwards, R.A.; Greenhalgh, J.F.D.; Morgan, C.A.; Sinclair, L.; Wilkinson, R.G. *Animal Nutrition*, 7th ed.; Pearson Education Limited: London, UK, 2011.
32. Galbraith, H. Hormones in international meat production: Biological, sociological and consumer issues. *Nutr. Res. Rev.* **2002**, *15*, 293–314. [CrossRef] [PubMed]
33. Davis, H.E.; Belk, K.E. Managing meat exports considering production technology challenges. *Anim. Front.* **2018**, *8*, 23–29. [CrossRef] [PubMed]
34. Reinhardt, C.D.; Wagner, J.J. High-dose anabolic implants are not all the same for growth and carcass traits of feedlot steers: A meta-analysis. *J. Anim. Sci.* **2014**, *92*, 4711–4718. [CrossRef]
35. Platter, W.J.; Tatum, J.D.; Belk, K.E.; Scanga, J.A.; Smith, G.C. Effects of repetitive use of hormonal implants on beef carcass quality, tenderness, and consumer ratings of beef palatability. *J. Anim. Sci.* **2003**, *81*, 984–996. [CrossRef]
36. Partridge, I. *Hormone Growth Promotants and Beef Production: A Best Practice Guide*; Meat and Livestock Australia Limited: Sydney, Australia, 2011.
37. Dunshea, F.R.; D'Souza, D.N.; Channon, H.A. Metabolic modifiers as performance-enhancing technologies for livestock production. *Anim. Front.* **2016**, *6*, 6–14. [CrossRef]

38. Zobell, D.R.; Chapman, C.K.; Heaton, K.; Birkelo, C. Beef cattle implants. In *All Archived Publications*; Utah State University Extension: Logan, UT, USA, 2000; Available online: https://digitalcommons.usu.edu/extension_histall/29/ (accessed on 3 February 2020).
39. Gifford, C.A.; Branham, K.A.; Ellison, J.O.; Gómez, B.L.; Lemley, C.O.; Hart, C.G.; Krehbiel, C.R.; Bernhard, B.C.; Maxwell, C.L.; Goad, C.L.; et al. Effect of anabolic implants on adrenal cortisol synthesis in feedlot beef cattle implanted early or late in the finishing phase. *Physiol. Behav.* **2015**, *138*, 118–123. [CrossRef]
40. Rokka, M.; Jestoi, M.; Peltonen, K. Trace level determination of polyether ionophores in feed. *Biomed. Res. Int.* **2013**, *2013*. [CrossRef]
41. Ranga Niroshan Appuhamy, J.A.D.; Strathe, A.B.; Jayasundara, S.; Wagner-Riddle, C.; Dijkstra, J.; France, J.; Kebreab, E. Anti-methanogenic effects of monensin in dairy and beef cattle: A meta-analysis. *J. Dairy Sci.* **2013**, *96*, 5161–5173. [CrossRef]
42. Duffield, T.F.; Merrill, J.K.; Bagg, R.N. Meta-analysis of the effects of monensin in beef cattle on feed efficiency, body weight gain, and dry matter intake. *J. Anim. Sci.* **2012**, *90*, 4583–4592. [CrossRef]
43. Goodrich, R.D.; Garrett, J.E.; Gast, D.R.; Kirick, M.A.; Larson, D.A.; Meiske, J.C. Influence of monensin on the performance of cattle. *J. Anim. Sci.* **1984**, *58*, 1484–1498. [CrossRef]
44. Spires, H.R.; Olmsted, A.; Berger, L.L.; Fontenot, J.P.; Gill, D.R.; Riley, J.G.; Wray, M.I.; Zinn, R.A. Efficacy of laidlomycin propionate for increasing rate and efficiency of gain by feedlot cattle. *J. Anim. Sci.* **1990**, *68*, 3382–3391. [CrossRef]
45. Thompson, A.J.; Smith, Z.K.; Corbin, M.J.; Harper, L.B.; Johnson, B.J. Ionophore strategy affects growth performance and carcass characteristics in feedlot steers. *J. Anim. Sci.* **2016**, *94*, 5341–5349. [CrossRef]
46. Hersom, M.; Thrift, T. *Application of Ionophores in Cattle Dets. IFAS Ext.*; University of Florida: Gainesville, FL, USA, 2012; Available online: https://edis.ifas.ufl.edu/pdffiles/AN/AN28500.pdf (accessed on 5 March 2020).
47. Centner, T.J.; Alvey, J.C.; Stelzleni, A.M. Beta agonists in livestock feed: Status, health concerns, and international trade. *J. Anim. Sci.* **2014**, *92*, 4234–4240. [CrossRef]
48. Neumeier, C.J.; Mitloehner, F.M. Cattle biotechnologies reduce environmental impact and help feed a growing planet. *Anim. Front.* **2013**, *3*, 36–41. [CrossRef]
49. Lean, I.J.; Thompson, J.M.; Dunshea, F.R. A meta-analysis of zilpaterol and ractopamine effects on feedlot performance, carcass traits and shear strength of meat in cattle. *PLoS ONE* **2014**, *9*, e115904. [CrossRef]
50. Smith, D.J.; Shelver, W.L.; Chakrabarty, S.; Hoffman, T.W. Detection and quantification of residues in sheep exposed to trace levels of dietary zilpaterol HCl. *Food Addit Contam Part A.* **2019**, *36*, 1289–1301. [CrossRef]
51. Maxwell, C.L.; Bernhard, B.C.; O'Neill, C.F.; Wilson, B.K.; Hixon, C.G.; Haviland, C.L.; Grimes, A.N.; Calvo-Lorenzo, M.S.; VanOverbeke, D.L.; Mafi, G.G.; et al. The effects of technology use in feedlot production systems on feedlot performance and carcass characteristics. *J. Anim. Sci.* **2015**, *93*, 1340–1349. [CrossRef] [PubMed]
52. Smith, Z.K.; Anderson, P.T.; Johnson, B.J. Finishing cattle in all-natural and conventional production systems. *Open J. Anim. Sci.* **2020**, *10*, 237–253. [CrossRef]
53. Kerr, W.A.; Hobbs, J.E. The North American-European union dispute over beef produced using growth hormones: A major test for the new international trade regime. *World Econ.* **2002**, *25*, 283–296. [CrossRef]
54. FAO. 2020. Available online: http://www.fao.org/faostat/en/#data (accessed on 25 March 2020).
55. Dilger, A. Beta-Agonists: What are They and Why Do We Use Them in Livestock Production. Available online: https://meatscience.org/docs/default-source/publications-resources/fact-sheets/beta-agonists---dilger-20158d82e7711b766618a3fcff0000a508da.pdf?sfvrsn=69f481b3_0 (accessed on 5 March 2020).
56. Organization for Economic Cooperation and Development. Meat Consumption (Indicator). 2020. Available online: https://data.oecd.org/agroutput/meat-consumption.htm (accessed on 31 January 2020).
57. Tait, P.; Rutherford, P.; Driver, T.; Li, X.; Saunders, C.; Dalziel, P.; Guenther, M. Consumer insights and willingness to pay for attributes: New Zealand beef products in California, USA. In *Agribusiness and Economics Research Unit Research*; Lincoln University New Zealand: Lincoln, New Zealand, 2018.
58. Beef Checkoff. When It Comes to Beef, Consumers Have Options. 2020. Available online: https://www.beefitswhatsfordinner.com/retail/sales-data-shopper-insights/options-at-retail (accessed on 16 August 2020).
59. Cheung, R.; McMahon, P.; Norell, E.; Kissel, R.; Benz, D.; Back to Grass: The Market Potential for U.S. Grass-Fed Beef. *Stone Barns Center for Food and Agriculture.* 2017. Available online: https://www.stonebarnscenter.org/wp-content/uploads/2017/10/Grassfed_Full_v2.pdf (accessed on 3 April 2020).
60. United States Department of Agriculture. *Statistics and Information*; United State Department of Agriculture: Washington, DC, USA, 2021. Available online: https://www.ers.usda.gov/topics/animal-products/cattle-beef/statistics-information.aspx (accessed on 14 January 2021).
61. Odde, K.G.; King, M.E.; McCabe, E.D.; Smith, M.J.; Hill, K.L.; Rogers, G.M.; Fike, K.E. Trends in "natural" value-added calf programs at superior livestock video auction. *Kansas Agric. Exp. Stn. Res. Reports* **2019**, *5*. [CrossRef]
62. Olvera, I.D. Economic Implications Associated with Pharmaceutical Technology Bans in U.S. Beef Production. Ph.D. Thesis, Texas A & M University, College Station, TX, USA, 2016.
63. White, R.R.; Brady, M. Can consumers' willingness to pay incentivize adoption of environmental impact reducing technologies in meat animal production? *Food Policy* **2014**, *49*, 41–49. [CrossRef]

64. Norris, A. Context Specific Factors Affecting Consumer Preferences for Antibiotic and Hormone Use during the Production of Beef in Canada. Master's Thesis, University of Guelph, Guelph, ON, Canada, 2020.
65. Lewis, K.E.; Grebitus, C.; Colson, G.; Hu, W. German and British consumer willingness to pay for beef labeled with food safety attributes. *J. Agric. Econ.* **2017**, *68*, 451–470. [CrossRef]
66. Colella, F.; Ortega, D.L. Where's the beef? Retail channel choice and beef preference in Argentina. *Meat Sci.* **2017**, *133*, 86–94. [CrossRef]
67. Hirvonen, K.; Bai, Y.; Headey, D.; Masters, W.A. Affordability of the EAT–Lancet reference diet: A global analysis. *Lancet Glob. Health* **2020**, *8*, e59–e66. [CrossRef]
68. Henchion, M.; Zimmermann, J. Animal food products: Policy, market and social issues and their influence on demand and supply of meat. *Proc. Nutr. Soc.* **2021**, 1–12. [CrossRef]
69. Charlebois, S.; Somogyi, S.; Music, J.; Caron, I. Planet, Ethics, Health and the New World Order in Proteins. *J. Agric. Stud.* **2020**, *8*, 171. [CrossRef]
70. Stackhouse-Lawson, K.R.; Calvo, M.S.; Place, S.E.; Armitage, T.L.; Pan, Y.; Zhao, Y.; Mitloehner, F.M. Growth promoting technologies reduce greenhouse gas, alcohol, and ammonia emissions from feedlot cattle. *J. Anim. Sci.* **2013**, *91*, 5438–5447. [CrossRef]
71. Cooprider, K.L.; Mitloehner, F.M.; Famula, T.R.; Kebreab, E.; Zhao, Y.; van Eenennaam, A.L. Feedlot efficiency implications on greenhouse gas sustainability. *J. Anim. Sci.* **2011**, *89*, 2643–2656. [CrossRef]
72. Capper, J.L. Is the grass always greener? Comparing the environmental impact of conventional, natural and grass-fed beef production systems. *Animals* **2012**, *2*, 127–143. [CrossRef]
73. Basarab, J.; Baron, V.; López-Campos, Ó.; Aalhus, J.; Haugen-Kozyra, K.; Okine, E. Greenhouse gas emissions from calf- and yearling-fed beef production systems, with and without the use of growth promotants. *Animals* **2012**, *2*, 195–220. [CrossRef]
74. Capper, J.L.; Hayes, D.J. The environmental and economic impact of removing growth-enhancing technologies from U.S. beef production. *J. Anim. Sci.* **2012**, *90*, 3527–3537. [CrossRef]
75. Stackhouse, K.R.; Rotz, C.A.; Oltjen, J.W.; Mitloehner, F.M. Growth-promoting technologies decrease the carbon footprint, ammonia emissions, and costs of California beef production systems. *J. Anim. Sci.* **2012**, *90*, 4656–4665. [CrossRef]
76. Webb, M.J. Influence of Production System on Animal Performance, Carcass Characteristics, Meat Quality, Environmental Impacts, Production Economics, and Consumer Preference for Beef. Ph.D. Thesis, South Dakota State University, Brookings, SD, USA, 2018.
77. Biswas, S.; Shapiro, C.A.; Kranz, W.L.; Mader, T.L.; Shelton, D.P.; Snow, D.D.; Bartelt-Hunt, S.L.; Tarkalson, D.D.; Van Donk, S.J.; Zhang, T.C.; et al. Current knowledge on the environmental fate, potential impact, and management of growth-promoting steroids used in the US beef cattle industry. *J. Soil Water Conserv.* **2013**, *68*, 325–336. [CrossRef]
78. Zhao, S.; Zhang, P.; Melcer, M.E.; Molina, J.F. Estrogens in streams associated with a concentrated animal feeding operation in upstate New York, USA. *Chemosphere* **2010**, *79*, 420–425. [CrossRef]
79. Hafner, S.C.; Harter, T.; Parikh, S.J. Evaluation of monensin transport to shallow groundwater after irrigation with dairylagoon water. *J. Environ. Qual.* **2016**, *45*, 480–487. [CrossRef]
80. Blackwell, B.R.; Wooten, K.J.; Buser, M.D.; Johnson, B.J.; Cobb, G.P.; Smith, P.N. Occurrence and characterization of steroid growth promoters associated with particulate matter originating from beef cattle feedyards. *Environ. Sci. Technol.* **2015**, *49*, 8796–8803. [CrossRef]
81. Wooten, K.J.; Sandoz, M.A.; Smith, P.N. Ractopamine in particulate matter emitted from beef cattle feedyards and playa wetlands in the Central Plains. *Environ. Toxic. Chem.* **2018**, *37*, 970–974. [CrossRef] [PubMed]
82. Challis, J.K.; Sura, S.; Cantin, J.; Curtis, A.W.; Shade, K.M.; McAllister, T.A.; Jones, P.D.; Giesy, J.P.; Larney, F.J. Ractopamine and other growth-promoting compounds in beef cattle operations: Fate and transport in feedlot pens and adjacent environments. *Environ. Sci. Technol.* **2021**, *55*, 1730–1739. [CrossRef] [PubMed]
83. Bartelt-Hunt, S.; Snow, D.D.; Damon-Powell, T.; Miesbach, D. Occurrence of steroid hormones and antibiotics in shallow groundwater impacted by livestock waste control facilities. *J. Contam. Hydrol.* **2011**, *123*, 94–103. [CrossRef] [PubMed]
84. Hanselman, T.A.; Graetz, D.A.; Wilkie, A.C. Manure-borne estrogens as potential environmental contaminants: A review. *Environ. Sci. Technol.* **2003**, *37*, 5471–5478. [CrossRef]
85. Henry, P.F.P.; Akuffo, V.G.; Chen, Y.; Karouna-Renier, N.K.; Sprague, D.T.; Bakst, M.R. Effect of 17β-trenbolone on male and female reproduction in Japanese quail (*Coturnix Japonica*). *Avian Biol. Res.* **2012**, *5*, 61–68. [CrossRef]
86. Quinn, M.J.; Lavoie, E.T.; Ottinger, M.A. Reproductive toxicity of trenbolone acetate in embryonically exposed Japanese quail. *Chemosphere* **2007**, *66*, 1191–1196. [CrossRef]
87. Shappell, N.W.; Hyndman, K.M.; Bartell, S.E.; Schoenfuss, H.L. Comparative biological effects and potency of 17 alpha- and 17 beta-estradiol in fathead minnows. *Aquatic. Toxicol.* **2010**, *100*, 1–8. [CrossRef]
88. Finch, B.E.; Blackwell, B.R.; Faust, D.R.; Wooten, K.J.; Maul, J.D.; Cox, S.B.; Smith, P.N. Effects of 17α-trenbolone and melengestrol acetate on *Xenopus laevis* growth, development, and survival. *Environ. Sci. Pollut. Res. Int.* **2013**, *20*, 1151–1160. [CrossRef]
89. Jeffries, K.M.; Jackson, L.J.; Ikonomou, M.G.; Habibi, H.R. Presence of natural and anthropogenic organic contaminants and potential fish health impacts along two river gradients in Alberta, Canada. *Environ. Toxicol. Chem.* **2010**, *29*, 2379–2387. [CrossRef]
90. Johns, S.M.; Denslow, N.D.; Kane, M.D.; Watanabe, K.H.; Orlando, E.F.; Sepúlveda, M.S. Effects of estrogens and antiestrogens on gene expression of fathead minnow (*Pimephales promelas*) early life stages. *Environ Toxicol.* **2011**, *26*, 195–206. [CrossRef]

91. Schwartz, P.; Thorpe, K.L.; Bucheli, T.D.; Wettstein, F.E.; Burkhardt-Holm, P. Short-term exposure to the environmentally relevant estrogenic mycotoxin zearalenone impairs reproduction in fish. *Sci. Total Environ.* **2010**, *409*, 326–333. [CrossRef]
92. Schwartz, P.; Bucheli, T.D.; Wettstein, F.E.; Burkhardt-Holm, P. Life-cycle exposure to the estrogenic mycotoxin zearalenone affects zebrafish (*Danio rerio)* development and reproduction. *Environ. Toxicol.* **2013**, *28*, 276–289. [CrossRef]
93. Adeel, M.; Song, X.; Wang, Y.; Francis, D.; Yang, Y. Environmental impact of estrogens on human, animal and plant life: A critical review. *Environ. Int.* **2017**, *99*, 107–119. [CrossRef]
94. Biswas, S.; Kranz, W.L.; Shapiro, C.A.; Snow, D.D.; Bartelt-Hunt, S.L.; Mamo, M.; Tarkalson, D.D.; Zhang, T.C.; Shelton, D.P.; van Donk, S.J.; et al. Effect of rainfall timing and tillage on the transport of steroid hormones in runoff from manure amended row crop fields. *J. Hazard Mater.* **2017**, *324*, 436–447. [CrossRef]
95. Havens, S.M.; Hedman, C.J.; Hemming, J.; Mieritz, M.G.; Shafer, M.M.; Schauer, J.J. Occurrence of estrogens, androgens and progestogens and estrogenic activity in surface water runoff from beef and dairy manure amended crop fields. *Sci. Total Environ.* **2020**, *710*, 136247. [CrossRef]
96. Leusch, F.D.L.; Neale, P.A.; Arnal, C.; Aneck-Hahn, N.H.; Balaguer, P.; Bruchet, A.; Escher, B.I.; Esperanza, M.; Grimaldi, M.; Leroy, G.; et al. Analysis of endocrine activity in drinking water, surface water and treated wastewater from six countries. *Water Res.* **2018**, *139*, 10–18. [CrossRef]
97. Pickford, D.B.; Jones, A.; Velez-Pelez, A.; Iguchi, T.; Mitsui, N.; Tooi, O. Screening breeding sites of the common toad (*Bufo bufo*) in England and Wales for evidence of endocrine disrupting activity. *Ecotoxicol. Environ. Saf.* **2015**, *117*, 7–19. [CrossRef]
98. Molina-Molina, J.M.; Real, M.; Jimenez-Diaz, I.; Belhassen, H.; Hedhili, A.; Torné, P.; Fernández, M.F.; Olea, N. Assessment of estrogenic and anti-androgenic activities of the mycotoxin zearalenone and its metabolites using in vitro receptor-specific bioassays. *Food Chem. Toxicol.* **2014**, *74*, 233–239. [CrossRef]
99. Bartelt-Hunt, S.L.; Snow, D.D.; Kranz, W.L.; Mader, T.L.; Shapiro, C.A.; Donk, S.J.; Shelton, D.P.; Tarkalson, D.D.; Zhang, T.C. Effect of growth promotants on the occurrence of endogenous and synthetic steroid hormones on feedlot soils and in runoff from beef cattle feeding operations. *Environ. Sci. Technol.* **2012**, *46*, 1352–1360. [CrossRef]
100. Amarakoon, I.D.; Zvomuya, F.; Sura, S.; Larney, F.J.; Cessna, A.J.; Xu, S.; McAllister, T.A. Dissipation of antimicrobials in feedlot manure compost after oral administration versus fortification after excretion. *J. Environ. Qual.* **2016**, *45*, 503–510. [CrossRef]
101. Carter, S.D.; Kim, H.J. Technologies to reduce environmental impact of animal wastes associated with feeding for maximum productivity. *Anim. Front.* **2013**, *3*, 42–47. [CrossRef]
102. Mersmann, H.J. Overview of the effects of beta-adrenergic receptor agonists on animal growth including mechanisms of action. *J. Anim. Sci.* **1998**, *76*, 160–172. [CrossRef] [PubMed]
103. Government of Canada. *Responsible Use of Medically Important Antimicrobials in Animals*; Government of Canada: Ottawa, AB, Canada, 2019; Available online: https://www.canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/animals/actions/responsible-use-antimicrobials.html (accessed on 19 August 2020).
104. Aidara-Kane, A.; Angulo, F.J.; Conly, J.; Minato, Y.; Silbergeld, E.K.; McEwen, S.A.; Collignon, P.J.; Balkhy, H.; Collignon, P.; Friedman, C.; et al. World Health Organization (WHO) guidelines on use of medically important antimicrobials in food-producing animals. *Antimicrob. Resist. Infect. Control* **2018**, *7*, 1–8. [CrossRef] [PubMed]
105. Global Roundtable for Sustainable Beef. Sustainability Report. 2018. Available online: https://grsbeef.org/resources/Documents/WhoWeAre/GRSB_Sustainability_Report_2018.pdf (accessed on 17 August 2020).
106. Wong, A. Unknown risk on the farm: Does Agricultural use of ionophores contribute to the burden of antimicrobial resistance? *mSphere* **2019**, *4*, 1–6. [CrossRef]
107. Baynes, R.E.; Dedonder, K.; Kissell, L.; Mzyk, D.; Marmulak, T.; Smith, G.; Tell, L.; Gehring, R.; Davis, J.; Riviere, J.E. Health concerns and management of select veterinary drug residues. *Food Chem. Toxicol.* **2016**, *88*, 112–122. [CrossRef]
108. FAO; WHO. Carryover in feed and transfer from feed to food of unavoidable and unintended residues of approved veterinary drugs. In *Report of the Joint FAO/WHO Expert Meeting from 8 to 10 January 2019*; Animal Production and Health; FAO: Rome, Italy, 2019.
109. Sakai, N.; Sakai, M.; Mohamad Haron, D.E.; Yoneda, M.; Ali Mohd, M. Beta-agonist residues in cattle, chicken and swine livers at the wet market and the environmental impacts of wastewater from livestock farms in Selangor State, Malaysia. *Chemosphere* **2016**, *165*, 183–190. [CrossRef]
110. Davis, H.E.; Badger, C.D.; Brophy, P.; Geornaras, I.; Burnett, T.J.; Scanga, J.; Belk, K.; Prenni, J. Quantification of ractopamine residues on and in beef digestive tract tissues. *J. Anim. Sci.* **2019**, *97*, 4193–4198. [CrossRef]
111. Arcella, D.; Baert, K.; Binaglia, M.; Gervelmeyer, A.; Innocenti, M.L.; Ribo, O.; Steinkellner, H.; Verhagen, H. Review of proposed MRLs, safety evaluation of products obtained from animals treated with zilpaterol and evaluation of the effects of zilpaterol on animal health and welfare. *EFSA J.* **2016**, *14*, e04579. [CrossRef]
112. Canadian Food Inspection Agency. *Canadian Beta Agonist-Free Beef Certification Program*; Government of Canada: Ottawa, AB, Canada, 2017; Available online: https://inspection.canada.ca/exporting-food-plants-or-animals/food-exports/food-specific-export-requirements/meat/annex-v/eng/1491926348345/1491926349115#b8 (accessed on 3 April 2020).
113. Australian Government Department of Agriculture. *National Residue Survey 2018–2019 Cattle*; Australian Government: Canberra, Australia, 2019. Available online: https://www.agriculture.gov.au/ag-farm-food/food/nrs/nrs-results-publications/industry-brochures/cattle (accessed on 25 May 2020).

114. USDA-Food Safety and Inspection Service. *Residue Sample Results—"Red Book"*; United State Department of Agriculture: Washington, DC, USA, 2019. Available online: http://www.fsis.usda.gov/wps/portal/fsis/topics/data-collection-and-reports/chemistry/red-books/red-book (accessed on 1 May 2020).
115. Groot, M.J.; Schilt, R.; Ossenkoppele, J.S.; Berende, P.L.; Haasnoot, W. Combinations of growth promoters in veal calves: Consequences for screening and confirmation methods. *Zentralbl. Veterinarmed. A.* **1998**, *45*, 425–440. [CrossRef]
116. Pérez-Martínez, C.; García-Iglesias, M.J.; Ferreras-Estrada, M.C.; Bravo-Moral, A.M.; Espinosa-Alvarez, J.; Escudero-Díez, A. Effects of in-utero exposure to zeranol or diethylstilboestrol on morphological development of the fetal testis in mice. *J. Comp. Pathol.* **1996**, *114*, 407–418. [CrossRef]
117. Biolatti, B.; Bollo, E.; Re, G.; Appino, S.; Tartari, E.; Benatti, G.; Elliott, C.T.; McCaughey, W.J. Pathology and residues in veal calves treated experimentally with clenbuterol. *Res. Vet. Sci.* **1994**, *57*, 365–371. [CrossRef]
118. Zimmerli, U.V.; Blum, J.W. Acute and long-term metabolic, endocrine, respiratory, cardiac and skeletal-muscle activity changes in response to perorally administered β-adrenoceptor agonists in calves. *J. Anim. Physiol. Anim. Nutr.* **1990**, *63*, 157–172. [CrossRef]
119. Neary, J.M.; Garry, F.B.; Gould, D.H.; Holt, T.N.; Dale Brown, R. The beta-adrenergic agonist zilpaterol hydrochloride may predispose feedlot cattle to cardiac remodeling and dysfunction [version 1; peer review: 2 approved with reservations]. *F1000Research* **2018**, *7*, 1–12. [CrossRef]
120. Loneragan, G.H.; Thomson, D.U.; Scott, H.M. Increased mortality in groups of cattle administered the β-adrenergic agonists ractopamine hydrochloride and zilpaterol hydrochloride. *PLoS ONE* **2014**, *9*, e91177. [CrossRef]
121. Huffstutter, P.J.; Polansek, T. *Lost Hooves, Dead Cattle before Merck Halted Zilmax Sales*; Reuters: London, UK, 2013.
122. Merck Animal Health. *Animal Safety and Well-Being*; Merck Animal Health: Madison, NJ, USA, 2015.
123. Carll, A.P.; Haykal-Coates, N.; Winsett, D.W.; Rowan, W.H., 3rd; Hazari, M.S.; Ledbetter, A.D.; Nyska, A.; Cascio, W.E.; Watkinson, W.P.; Costa, D.L.; et al. Particulate matter inhalation exacerbates cardiopulmonary injury in a rat model of isoproterenol-induced cardiomyopathy. *Inhal. Toxicol.* **2010**, *22*, 355–368. [CrossRef]
124. Chiarella, S.E.; Soberanes, S.; Urich, D.; Morales-Nebreda, L.; Nigdelioglu, R.; Green, D.; Young, J.B.; Gonzalez, A.; Rosario, C.; Misharin, A.V.; et al. β2-Adrenergic agonists augment air pollution-induced IL-6 release and thrombosis. *J. Clin. Investig.* **2014**, *124*, 2935–2946. [CrossRef]
125. Neary, J.M.; Booker, C.W.; Wildman, B.K.; Morley, P.S. Right-sided congestive heart failure in North American feedlot cattle. *J. Vet. Intern. Med.* **2016**, *30*, 326–334. [CrossRef]
126. Frese, D.A.; Reinhardt, C.D.; Bartle, S.J.; Rethorst, D.N.; Bawa, B.; Thomason, J.D.; Loneragan, G.H.; Thomson, D.U. Effect of ractopamine hydrochloride and zilpaterol hydrochloride on cardiac electrophysiologic and hematologic variables in finishing steers. *J. Am. Vet. Med. Assoc.* **2016**, *249*, 668–677. [CrossRef]
127. Hagenmaier, J.A.; Reinhardt, C.D.; Ritter, M.J.; Calvo-Lorenzo, M.S.; Vogel, G.J.; Guthrie, C.A.; Siemens, M.G.; Lechtenberg, K.F.; Rezac, D.J.; Thomson, D.U. Effects of ractopamine hydrochloride on growth performance, carcass characteristics, and physiological response to different handling techniques. *J. Anim. Sci.* **2017**, *95*, 1977–1992. [CrossRef]
128. United State Food and Drug Administration (FDA). *FDA Approves Experior for Reduction of Ammonia Gas Released from Beef Cattle Waste*; Center for Veterinary Medicine: Lewisville, TX, USA, 2018.
129. Government of Canada. *Lubabegron—Medicating Ingredient Brochure*; Government of Canada: Ottawa, AB, Canada, 2021; Available online: https://inspection.canada.ca/animal-health/livestock-feeds/medicating-ingredients/lubabegron/eng/1547583000099/1547583001862 (accessed on 23 March 2021).
130. Workman, D. Top Beef Exporting Countries. Available online: http://www.worldstopexports.com/top-beef-exporting-countries/ (accessed on 1 June 2020).
131. Government of Canada. *Text of the Comprehensive Economic and Trade Agreement—Annex 2-A: Tariff Elimination*; Government of Canada: Ottawa, AB, Canada, 2017; Available online: https://www.international.gc.ca/trade-commerce/trade-agreements-accords-commerciaux/agr-acc/ceta-aecg/text-texte/02-A.aspx?lang=eng (accessed on 1 June 2020).
132. Teel, G. *CCA Cheers Declaration of Complete CETA Text*; Canadian Cattlemen's Association (CCA): Calgary, AB, Canada, 2014; Available online: https://www.cattle.ca/assets/Article/d34f9112f1/09-26-2014-CCA-cheers-declaration-of-complete-CETA-text2.pdf (accessed on 1 June 2020).
133. Arnason, R. *EU Trade Deal Falls Short of Promises for Beef Producers*; The Western Producer: Saskatoon, SK, Canada, 2020.
134. United States Department of Agriculture. *Export Requirements for The People's Republic of China*; United State Department of Agriculture: Washington, DC, USA, 2020. Available online: https://www.fsis.usda.gov/wps/portal/fsis/topics/international-affairs/exporting-products/export-library-requirements-by-country/peoples-republic-of-china (accessed on 30 May 2020).