



THE CONTRIBUTION OF ANTHROPOSOPHIC MEDICINE TO ADDRESSING THE PROBLEM OF ANTIMICROBIAL RESISTANCE (AMR)

IVAA POSITION PAPER ON ANTIMICROBIAL RESISTANCE (AMR)
2021 UPDATE

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INTRODUCTION

This position paper is an update to IVAA's position paper on antimicrobial resistance (AMR) released in 2017 prior to the publication of the European Commission's One Health Action Plan against AMR and the EU4Health Programme 2021-2028. This update considers the recent developments in national, European, and international policies addressing the SARS-CoV-2 (COVID-19) outbreak and its effects on AMR.

SUMMARY IVAA'S RECOMMENDATIONS

Studies show the significant potential from Anthroposophic and other Integrative Medicine approaches to safely reduce antimicrobial resistance (AMR). Therefore:

- POLICY Anthroposophic Medicine and other Integrative Medicine approaches should be included as promising options in European and international policies to prevent AMR and reduce antibiotic use.
- HEALTHCARE SYSTEMS Processes of health promotion¹ and patient resilience should be included as strategies of prevention in national public health strategies and in National Action Plans (NAPs) on AMR.
- PATIENT INFORMATION AND EDUCATION Public education on reducing antibiotic use in health services should include options of evidence-based Integrative Medicine approaches in prevention and treatment of infectious diseases.
- **RESEARCH & DEVELOPMENT** Further evaluation and research on Anthroposophic and Integrative Medicine approaches on AMR should be further prioritized and supported in academic and research institutions. Outcomes should be shared with healthcare professionals, policy makers, stakeholders and public through appropriate tools.
- ONE HEALTH APPROACH The One Health approach and the collaboration between human, animal, and plant sectors should be fostered on regional, national, and international level to effectively prevent AMR in an environmentally sustainable way.

¹ Health promotion is the process of enabling people to increase control over, and to improve their health. Reference: Ottawa Charter for Health Promotion. WHO, Geneva, 1986. https://www.who.int/teams/health-promotion/enhanced-wellbeing/first-global-conference

ANTIMICROBIAL RESISTANCE TODAY: A ONE HEALTH CHALLENGE²

The World Health Organization (WHO) declared antimicrobial resistance (AMR) – the ability of microorganisms to resist antibiotic, antiviral, antifungal and antiparasitic medicines³ – as one of the ten major global public health threats facing humanity⁴. Infections caused by multi-resistant bacteria are predicted to be a leading cause of death by 2050⁵, adding further pressure on healthcare systems around the world. Currently, infections caused by multi-resistant bacteria in the EU/EEA countries is responsible for about 33 000 deaths and leads to additional healthcare costs of about 1.1 billion Euros each year⁶. The World Bank⁷ predicts a loss of 3.8% annual GDP by 2050, with a global additional health expenditure of 1.2 trillion USD per year due to the rise of AMR.

AMR is a major global health crisis that affects not only humans but also animals, plants and the environment and thus should be tackled with a **One Health approach**, by multisectoral fields⁸. Major contributors to the development of multiresistant bacteria are the over- and misuse of antibiotics in both humans and animals, including the agricultural and animal husbandry sector⁹. Another aggravator of AMR is the direct discharge of waste products from pharmaceutical production plants and hospitals into water bodies¹⁰. Multi-resistant bacteria derived in outpatient care and the animal health industry became highly prevalent, posing a heightened risk to patients with multimorbidity and immunosuppression, or lifethreatening infections. Aggressive antibiotic regimens in

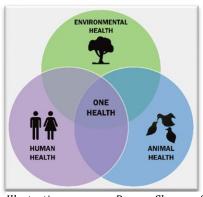


Illustration source: Deem, Sharon & Brenn-White, Maris. (2020). One Health – the Key to Preventing COVID-19 from Becoming the New Normal. Molecular Frontiers Journal. 04. 10.1142/S2529732520400039.

² The concept of One Health was defined in the Political Declaration of the high level meeting of the General Assembly on antimicrobial resistance of the United Nations as "the integrative effort of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals and the environment" United Nations, 'Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance', United Nations, New York, N.Y. (USA), 2016: http://digitallibrary.un.org/record/842813/files/A_71_L-2-EN.pdf

³ While the paper references mostly antibiotics instead of antimicrobials, as the elimination of antibiotic resistance is at the highest interest of all involved stakeholders.

⁴ World Health Organization, 2020: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

⁵ Final report and recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance, 2019: https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdfsfvrsn=5b424d7 6

⁶ Briefing note for EU/EEA countries by the Organisation for Economic Co-operation and Development (OECD) and the European Centre for Disease Prevention and Control (ECDC), 2019: Antimicrobial Resistance Tackling the Burden in the European Union: https://www.oecd.org/health/health-systems/AMR-Tackling-the-Burden-in-the-EU-OECD-ECDC-Briefing-Note-2019.pdf

The World Bank, 2017: Drug-resistant infections. A Threat to Our Economic Future: https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf

⁸ European Medicines Agency, 2019: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-antimicrobial-resistance-environment-considerations-current-future-risk-assessment_en.pdf

⁹ COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL AND THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE, 2019: European Union Strategic Approach to Pharmaceuticals in the Environment COM(2019) 128 final:

https://ec.europa.eu/environment/water/water-dangersub/pdf/strategic approach pharmaceuticals env.PDF

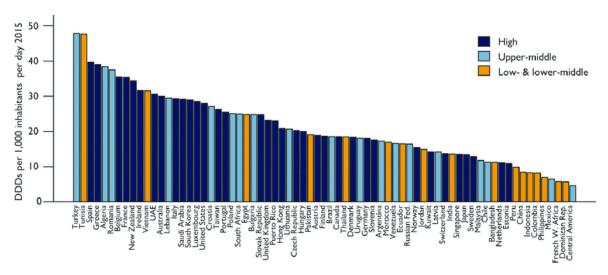
¹⁰ Pieper, U. & von Hildebrand, A. & Tisocki, K. (2020). Call for a Sound Management of Pharmaceutical Waste and Wastewater to Curb Antimicrobial Resistance:

https://www.researchgate.net/publication/344026638 Call for a Sound Management of Pharmaceutical Waste and Waste water to Curb Antimicrobial Resistance

hospitals and the low threshold for antibiotic use are leading to the development of multiresistant bacteria, increasing hospital acquired infections with AMR¹¹.

The recent emergence of the SARS-CoV-2 (COVID-19) pandemic accelerated the threat of antimicrobial resistance¹², adding further pressure on healthcare to develop effective AMR stewardship practices¹³. A review of 18 studies published on SARS-CoV-2 (COVID-19) patients found that 72% of the patients received antimicrobial therapy, while only 8% showed superimposed bacterial or fungal co-infections¹⁴.

AMR also threatens the effective use of currently existing antibiotics¹⁵: due to the development of resistance to first-line antibiotics¹⁶, the global per capita consumption of second-line watch antibiotics, reserved for multidrug-resistant infections, has increased by 90.9% between 2000-2015¹⁷. This is largely due to antibiotic consumption rates of Low- and Middle-Income Countries, where a 165% increase has been observed in the same period.



Global antibiotic consumption by country: 2015. Source: Klein, E.Y. et al. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proceedings of the National Academy of Sciences. 115(15): E3463-E3470: doi:10.1016/S1473-3099(20)30332-7. Fig. 1.

¹¹ Friedrich, A.W. (2019). Control of hospital acquired infections and antimicrobial resistance in Europe: the way to go. Wien Med Wochenschr. 2019 Feb;169(Suppl 1):25-30: doi:10.1007/s10354-018-0676-5

¹² Getahun, H., Smith, I., Trivedi, K., Paulina, S. & Balkhyb, H.H. (2020). Tackling antimicrobial resistance in the COVID-19 pandemic. *Bull World Health Organ* 2020;98:442–442A: doi: http://dx.doi.org/10.2471/BLT.20.268573

¹³ E.g., Mazdeyasna, H., Nori, P., Patel, P. et al. (2020). Antimicrobial Stewardship at the Core of COVID-19 Response Efforts: Implications for Sustaining and Building Programs. *Curr Infect Dis Rep 22, 23*: https://doi.org/10.1007/s11908-020-00734-x

¹⁴ Rawson, T.M., Moore, L.S.P., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., et al. (2020). Bacterial and fungal coinfection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.;ciaa530*: doi: http://dx.doi.org/10.1093/cid/ciaa530

¹⁵ The Center for Disease Dynamics, Economics & Policy (CDDEP), 2021: The State of the World's Antibiotics 2021. A Global Analysis of Antimicrobial Resistance and Its Drivers: https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf

¹⁶ According to the Access, Watch, and Reserve (AwaRe) antibiotic classification system developed by the World Health Organization (WHO, 2019) "access antibiotics are those that can treat a wide range of common pathogens and have lower resistance potential and should therefore be considered first-line options over antibiotics in the other categories. Watch antibiotics are those with higher resistance potential and those deemed "critically important antimicrobials for human medicine. [...] Reserve antibiotics should be used only for multidrug-resistant infections that cannot be treated by any other antibiotic.": https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf

¹⁷ Klein, E. Y. et al. (2021). Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. *Lancet Infect. Dis. 21*, 107–115: doi:10.1016/S1473-3099(20)30332-7

POLICIES TACKLING ANTIMICROBIAL RESISTANCE

The 2015 World Health Organization's global action to tackle antimicrobial resistance¹⁸ identifies AMR as a multi-sectoral threat that directly impacts 7 of the 17 sustainable development goals (SDGs)¹⁹. In the past decade, several national and international strategies have been adopted to tackle AMR²⁰. On a European level, the following policies and projects were issued:





¹⁸ World Health Organization, 2015: Global Action Plan on Antimicrobial Resistance. Available through www.who.intl

¹⁹ https://www.who.int/antimicrobial-resistance/interagency-coordination-group/AMR SDG indicators analysis slides.pdf

 $^{^{\}rm 20}$ World-Health-Organization. Global action plan on antimicrobial resistance. 2015.

²¹ EU Joint Action on AMR and Healthcare-Associated Infections, 2017: https://eu-jamrai.eu/vision-mision/#

²² MEPs fight AMR: MEP Interest Group on Antimicrobial Resistance: https://epha.org/amr-interest-group/

²³ MEP Interest Group on AMR, 2019: 2019-2024 strategic work programme: https://epha.org/wp-content/uploads/2020/02/mep-vs-amr-work-programme.pdf



European Commission

2017



The EU One Health Action Plan against Antimicrobial Resistance (AMR)²⁴ has three main pillars: making the EU a best practice region; boosting research, development and innovation as well as shaping the global agenda²⁵.

2020



The EU4Health 2021-2027 programme²⁶ includes suggestions for the prudent and efficient use of antimicrobials while furthering development and actions of environmentally friendly production and disposal of medicinal products, in accordance with the One Health approach of the Commission's Action Plan against AMR.

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²⁴ European Comission, 2017. Communication from the Commission to the Council and the European Parliament: A European One Health Action Plan against Antimicrobial Resistance (AMR): https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52017DC0339

European Commission, 2021 Q2. Progress Report: 2017 EU AMR Action Plan: https://ec.europa.eu/health/sites/default/files/antimicrobial resistance/docs/amr 2018-2022 actionplan progressreport en.pdf

²⁶ Regulation (EU) 2021/522 of the European Parliament and of the Council of 24 March 2021 establishing a Programme for the Union's action in the field of health ('EU4Health Programme') for the period 2021-2027, and repealing Regulation (EU) No 282/2014: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R0522&from=EN

Global Level









The Tripartite Joint Secretariat on Antimicrobial Resistance is a consolidated cooperation between the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Organisation for Animal Health (OIE), drawing on their core mandate and comparative advantages to address the wide range of needs of the global response against AMR²⁷.



The establishment of the **Global Leaders Group on Antimicrobial Resistance**²⁸ was recommended by the Interagency Coordination Group (IACG) on Antimicrobial Resistance. The Global Leaders Group includes members from Member States, civil society and the private sector, with the aim to strengthen global political momentum and leadership on AMR.



Call to Action on Antimicrobial Resistance (AMR) - 2021²⁹: Presented by the Group of Friends on Tackling AMR on 29 April 2021 to raise global ambition on AMR whilst accommodating diverse national circumstances. The group is calling for enhanced national and global efforts to tackle AMR through a One Health approach; the acceleration of previous commitments to tackle AMR; improved antimicrobial stewardship; for work towards financing for AMR action; increased research on AMR's impacts; and for supporting the new One Health Global Leaders Group on AMR among other key steps. As of 30 July 2021, 113 Member States signed the Call to Action with 29 supporting organisations.

 $^{{}^{28}\,}Global\,Leaders\,Group\,on\,Antimicrobial\,Resistance,\,2020:\,\underline{https://www.who.int/groups/one-health-global-leaders-group-on-antimicrobial-resistance}$

²⁹ Group of Friends on Tackling AMR, 2021: https://www.un.org/pga/75/wp-content/uploads/sites/100/2021/04/Call-to-Action-on-Antimicrobial-Resistance-AMR-2021.pdf

While it is promising that an analysis showed a significant decrease of antibiotic consumption rates in EU/EEA between 2010-2019³⁰, currently these strategies appear insufficient with significant discrepancies prevalent in antibiotic consumption rates in EU countries. The State of the World's Antibiotics Report in 2021³¹ published by the Center For Disease Dynamics, Economics & Policy highlights that with current global trends, antibiotic consumption rates will double between 2015-2030³².

To effectively tackle AMR at global, regional, and national level, comprehensive approaches should reduce the need for and the consumption of antibiotics, while seeking out for non-antibiotic prevention and treatment methods. While prevention and control strategies include vaccines, better diagnostics, and surveillance along the development of new antibiotics, research and implementation of Integrative Medicine therapies are also needed³³.

ANTHROPOSOPHIC MEDICINE AND INTEGRATIVE MEDICINE



Photo source: Filderklinik

Integrative Medicine (IM) denotes the integration of conventional medicine with complementary and traditional medicine approaches.

Anthroposophic Medicine (AM) is an integrative medicine system based on a holistic understanding of man and disease, that is practiced additionally to and in integration with conventional medicine³⁴. Anthroposophic Medicine practiced by medical practitioners therapists and trained Anthroposophic Medicine.

Anthroposophic approaches are also applied in veterinary medicine and biodynamic farming. Anthroposophic Medicine aims to treat patients by supporting and strengthening the self-healing ability of human organisms when coping with diseases. This includes restricted use of antibiotics and antipyretics in infections³⁵, use of natural medicinal products and non-medicinal treatments, such as external embrocation and compresses. There is promising evidence that the

 $^{^{30}}$ European Center for Disease Prevention and Control, 2019: $\underline{\text{https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2019}$

 $^{^{31}}$ The Center for Disease Dynamics, Economics & Policy (CDDEP), 2021: $\underline{\text{https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf}$

³² Klein, E. Y. et al. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc. Natl. Acad. Sci. U. S. A. 115*, E3463–E3470: https://doi.org/10.1073/pnas.1717295115

³³ In most global, regional and national AMR policies, six main strategies are used to reduce AMR: infection prevention and control of resistant bacteria; monitoring of both infection prevention and control of resistant bacteria; research on antibiotic resistance and antibiotic use; appropriate use of antibiotics (e.g. not for viral infections); less antibiotic use (e.g. delayed prescription and alternatives); and development of new antibiotics. Baars, E., Belt, E., von Ammon, K., Breitkreuz, T., von Flotow, P., Huber, R., van Leeuwen, W., Martin, D., Matthes, H., Vagedes, J., van der Werf, E., & Willcox, M. (2018). Reducing the need for antibiotics The contribution of Complementary and Alternative Medicine. In E. Baars, E. Belt, P. von Flotow, T. Nicolai, & M. Smith (Eds.), Appropriate use of antibiotics: the role of CAM treatment strategies pp. 40. EUROCAM. www.cam-europe.eu

³⁴ Kienle, G.S., Albonico, H.-U., Baars, E., et al. (2013). Anthroposophic Medicine: an integrative medical system originating in Europe. *Glob Adv Health Med.*;2(6):20-31: doi:10.7453/gahmj.2012.087

³⁵ Martin, D. (2016). Fever: Views in Anthroposophic Medicine and Their Scientific Validity. *Evid Based Complement Alternat Med.*, 13: doi:10.1155/2016/3642659

integrative medical approach, including integrative medicinal products, increases both patient satisfaction and overall health outcomes, addressing global health challenges in a One Health approach.

THE CONTRIBUTION OF ANTHROPOSOPHIC MEDICINE TO REDUCE THE THREAT OF AMR

The concept of health promotion and infection prevention strategies lie at the heart of Anthroposophic and Integrative Medicine³⁶ and should be – alongside preventive medicine, surveillance, vaccine and new antibiotic development – at the core of any strategy tackling infectious diseases. Health promotion aims towards a state of optimal health, a naturally reinforced immune system, and a stronger health resilience.



Photo source: Filderklinik

Integrative Medicine contributes to

reducing the threat of AMR through patient-centred, health system oriented, effective prevention strategies, avoiding the misuse and overuse of antimicrobials, the two main drivers in the development of drug-resistant pathogens³⁷. Anthroposophic and Integrative Medicine support the One Health approach by extending their practice into multi-sectoral fields.

Reducing antibiotic use is difficult: reductions by only 5-12 percentage points³⁸ have been reported from conventional intervention studies³⁹. There is promising evidence that antibiotic prescription rates of health practitioners working with integrative methods can be dramatically lower than those of conventional physicians, while ensuring positive patient satisfaction as well as equivalent outcomes and safety⁴⁰. Effective and safe non-antibiotic treatment of infections is one of the strategies to reduce inappropriate use of antibiotics; the following studies show that the integrative approach, which aims to strengthen humans' and animals' resilience to infections, can lead to the prescription and consumption of fewer antibiotics, some of which treatment strategies have been shown to be effective also in systematic reviews:

³⁶ Baars, E. W., Zoen, E. B., Breitkreuz, T., Martin, D., et. al. (2019). The Contribution of Complementary and Alternative Medicine to Reduce Antibiotic Use: A Narrative Review of Health Concepts, Prevention, and Treatment Strategies. *Evidence-Based Complementary and Alternative Medicine*, 5365608: https://doi.org/10.1155/2019/5365608

³⁷ World Health Organization, 13 October 2020: Antimicrobial Resistance. HYPERLINK "https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance": https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

³⁸ Meeker, D., Linder, J.A., Fox, C.R., et al. (2016). Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: A randomized clinical trial. *JAMA*, 315(6):562-570: doi:10.1001/jama.2016.0275

³⁹ Little, P., Stuart, B., Francis, N., et al. (2013). Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. *Lancet*, *382*(9899):1175-1182: doi:10.1016/S0140-6736(13)60994-0

 $^{^{40}}$ For reference see footnote nr. 36

2020

31510

An app-based registry⁴¹ collecting data on febrile infections showed that effective and directed fever management strategies⁴² significantly reduce the need for the use of pyrectics and antibiotics.

Annagaet

A prospective nonrandomized, comparative study⁴³ showed that the frequency of antibiotic use and need for surgical intervention in the treatment of children with chronic otitis media with effusion was significantly lower using integrative-anthroposophic treatment (17.9% vs. 82.9%, with a reduction of the need for antibiotic treatments per year from 1.5 to 0.5 treatments)⁴⁴, which was confirmed in a 2020 follow up study⁴⁵.



In a retrospective study on the use of antibiotics in children hospitalised with pneumonia (lung infection) in the Filderklinik, a hospital in Germany that integrates conventional with Anthroposophic Medicine, only 32% of children required antibiotics⁴⁶, much lower than rates reported in the scientific literature, 88–98 %. Safety and outcomes were excellent in the study.



Uncomplicated, acute respiratory tract infections (RTIs) in many EU countries demonstrate entry points for delayed prescription and options for Integrative Medicine treatments: Reducing the use of antibiotics in primary care and counteracting the development of AMR are pressing international priorities⁴⁷. For example, in a prospective comparison of outcomes in patients with upper respiratory infections and ear infections under real-world conditions, a difference in antibiotic prescribing rates of 28 percentage points was noted

 $^{^{41}}$ Martin, D., Wachtmeister, J., Ludwigs, K., & Jenetzky, E. (2020). The FeverApp registry - Ecological momentary assessment (EMA) of fever management in families regarding conformity to up-to-date recommendations. *BMC Medical Informatics and Decision Making*, 20(1), 1–8: https://doi.org/10.1186/s12911-020-01269-w

⁴² For reference see footnote nr. 35

⁴³ Szoke, H., Marodi, M., Sallay, Z., Szekely, B., Sterner, M.-G., and Hegyi, G. (2016). Integrative versus Conventional Therapy of Chronic Otitis Media with Effusion and Adenoid Hypertrophy in Children: A Prospective Observational Study. *Forschende Komplementärmedizin*, 23(4), 231–239: doi:10.1159/000448440

⁴⁴ The P.E.A.N.U.T. is a multimodal method developed in 2013 in Hungary, to reduce antibiotic use and need for surgical interventions in chronic otitis media in childhood. The method is efficient, safe, and cost-effective, easy to perform in different clinical settings. It involves the following six elements: Pneumatization exercises; Education of patients and parents; an Antiallergic diet; Nasal hygiene; Useful constitutional therapy; and Thermal interventions.

⁴⁵ Szoke, H., Marodi, M., Vagedes, J., Szekely, B., Magyarosi, I., Bedo, A., Fellegi, V., Somogyvari, K., & Moricz, P. (2021). The P.E.A.N.U.T.. method: Update on an integrative system approach for the treatment of chronic otitis media with effusion and adenoid hypertrophy in children. *Antibiotics*, 10(2), 1–14: doi.org/10.3390/antibiotics10020134

⁴⁶ Vagedes, J., Martin, D., Müller, V., Helmert, E., Huber, B. M., Andrasik, F., & von Schoen-Angerer, T. (2020). Restrictive antibiotic use in children hospitalized for pneumonia: A retrospective inpatient study. *European Journal of Integrative Medicine, 34, 101068:* https://doi.org/10.1016/j.eujim.2020.101068

⁴⁷ Baars, E. W., Belt-Van Zoen, E., Willcox, M., Huber, R., Hu, X. Y., & van der Werf, E. T. (2020). CAM treatments for cough and sore throat as part of an uncomplicated acute respiratory tract infection: a systematic review of prescription rates and a survey among European integrative medical practitioners. *European Journal of Integrative Medicine, 39*(April), 101194: https://doi.org/10.1016/j.eujim.2020.101194

(5.5% if treated by an anthroposophic physician, 33.6% if treated by a conventional physician)⁴⁸.



Low antibiotic prescription rates have been found among physicians practicing other Integrative Medicine approaches⁴⁹. These findings are supported by a cohort study in France between 2007 and 2008⁵⁰.



2019

2016

Lower antibiotic use may reflect both physician and client preferences⁵¹: in a cross-sectional study including 6,630 children, 41.6% of children of parents with preferences for Anthroposophic Medicine never had antibiotic treatments compared to only 15.1% of reference children⁵².



NHS England GP surgeries employing GPs additionally trained in IM/CAM have lower antibiotic prescribing rates: Negative binomial regression models showed that statistically significant fewer total antibiotics (relative risk (RR) 0.78, 95% CI 0.64 to 0.97) and RTI antibiotics (RR 0.74, 95% CI 0.59 to 0.94) were prescribed at NHS IM GP surgeries compared with conventional NHS GP surgeries, according to the analysis of NHS Digital data over 2016⁵³.



Reduced anti-pyretic use⁵⁴, as practiced in Anthroposophic Medicine, may contribute to reducing infection rates⁵⁵. A secondary analysis of the above study with 529 children showed that antibiotics were prescribed to 5.5% of children treated by anthroposophic doctors and 25.6% children treated in conventional settings⁵⁶.

⁴⁸ Hamre, H.J., Fischer, M., Heger, M., et al. (2005). Anthroposophic vs. conventional therapy of acute respiratory and ear infections: a prospective outcomes study. *Wien Klin Wochenschr*, *117*(7-8):256-268: doi:10.1007/s00508-005-0344-9

⁴⁹ For reference see footnote nr. 36

⁵⁰ Grimaldi-Bensouda, L., Bégaud, B., Rossignol, M., et al. (2014). Management of upper respiratory tract infections by different medical practices, including homeopathy, and consumption of antibiotics in primary care: the EPI3 cohort study in France 2007–2008. *PLoS One, 9*(3):e89990: doi:10.1371/journal.pone.0089990

⁵¹ For reference see footnote nr. 36

⁵² Flöistrup, H., Swartz, J., Bergstrom, A., et al. (2006). Allergic disease and sensitization in Steiner school children. *J Allergy Clin Immunol*, 117(1):59-66: doi:10.1016/j.jaci.2005.09.039

⁵³ Kok, E. & Duncan, L. & von Flotow, P. & Baars, E. (2018). Do NHS GP surgeries employing GPs additionally trained in integrative or complementary medicine have lower antibiotic prescribing rates? Retrospective cross-sectional analysis of national primary care prescribing data in England in 2016. *BMJ Open*, 8(3):e020488: doi:10.1136/bmjopen-2017-020488.

 $^{^{54}}$ Earn, D.J.D., Andrews, P.W. & Bolker, B.M. (2014). Population-level effects of suppressing fever. Proceedings of the Royal Society B: Biological Sciences, 281(1778):20132570: $\frac{1}{2} \frac{1}{2} \frac{1}{$

⁵⁵ For reference see footnote nr. 35

⁵⁶ Hamre, H.J., Glockmann, A., Schwarz, R., et al. (2014). Antibiotic use in children with acute respiratory or ear infections: prospective observational comparison of anthroposophic and conventional treatment under routine primary care conditions. *Evidence-Based Complementary and Alternative Medicine*, 2014:243801: doi:10.1155/2014/243801

RECOMMENDATIONS AND FUTURE PERSPECTIVES

Given the magnitude of the AMR problem, all promising options that can mitigate the risk of AMR must be considered, including the potential of the Anthroposophic Medicine and other Integrative Medicine approaches.

IVAA recommends the following actions:

- **POLICY** Anthroposophic Medicine and other Integrative Medicine approaches should be included as promising policies to reduce antibiotics use and mitigate the risk of AMR, including in the European Commission's second AMR EU One Health Action Plan.
- HEALTHCARE SYSTEMS Evaluating the potential of Anthroposophic and Integrative Medicine prevention and treatment strategies in symptom relief and reducing antibiotic use should be prioritized and supported in National Action Plans (NAPs) on AMR. Adoption and implementation of processes of health promotion and patient resilience with the involvement all healthcare practitioners and therapists, in national AMR stewardship practices would further reduce the threat of AMR healthcare institutions. Background: Prescription and dispensing behaviour in primary care accounts as one of the main drivers of AMR with at least 80% of antibiotics being prescribed in primary care⁵⁷. Consumption targets should be considered to "reduce inappropriate prescribing practices and support improved control mechanisms to ensure these targets are effectively met"58.
 - a. Evaluations should include enhancing the practice of delayed prescription of antibiotics⁵⁹ with the addition of Anthroposophic and Integrative Medicine approaches⁶⁰.
 - b. Expertise of Anthroposophic and other Integrative Medicine specialists regarding risk management, reduction of prescription and consumption rates should be shared through appropriate tools.
 - c. Enhance the collaboration among health care professionals to fight AMR: all healthcare professions (e.g., physicians, pharmacists, nurses, therapists) must be involved in an AMR strategies and implementation of AMR stewardship practices.

⁵⁷ Rebnord, I. K., Sandvik, H., Mjelle, A. B., & Hunskaar, S. (2017). Factors predicting antibiotic prescription and referral to hospital for children with respiratory symptoms: secondary analysis of a randomised controlled study at out-of-hours services in primary care. *BMJ open, 7*(1), e012992: doi:10.1136/bmjopen-2016-012992

⁵⁸ European Public Health Alliance, October 5, 2020: The Pharmaceutical Strategy is a chance to tackle antimicrobial resistance that Europe cannot miss says the MEP Interest Group on AMR: https://epha.org/pharmaceutical-strategy-is-chance-to-tackle-antimicrobial-resistance-says-mep-interest-group-on-amr/

⁵⁹ <u>A review of studies</u>, published in BMJ in 2021, suggests that delayed prescribing may also be a safe and effective approach for treating most respiratory tract infections. For their analysis, researchers combined individual patient data on more than 55,000 people in nine randomized controlled trials and four observational studies. Stuart, B., Hounkpatin, H., Becque, T., et al. (2021). Delayed antibiotic prescribing for respiratory tract infections: individual patient data meta-analysis. BMJ (Clinical research ed.), 373, n808: https://doi.org/10.1136/bmj.n808

⁶⁰ Geyer, U., Diederich, K., Kusserow, M., Laubersheimer, A., & Kramer, K. (2013). Inpatient Treatment of Community-Acquired Pneumonias with Integrative Medicine. *Evidence-Based Complementary and Alternative Medicine, Special issue*: https://doi.org/10.1155/2013/578274

PATIENT INFORMATION AND EDUCATION Public education in the prevention and treatment of infectious diseases should include suggestion of evidence based Anthroposophic and Integrative Medicine approaches, both for healthcare professionals and patients. Particular attention should be made to hospital patients and paediatric patients.

Background: Promotion of lifestyle changes which support an effective immune system can prevent from and help fight infectious diseases. Interventions can be achieved through the distribution of information provided to patients and health care staff. By focusing on health promotion and disease prevention, Integrative Medicine approaches enable patients to exert control over their health and enhance patient's resilience 61 .

- d. Healthcare professionals should be trained on the appropriate use of evidence based Anthroposophic and Integrative Medicine approaches prevention and treatment of infectious diseases.
- e. Knowledge and guidelines in prevention and treatment of infectious diseases should include suggestion of evidence based Anthroposophic and Integrative Medicine approaches should be shared with both health care staff and patients e.g., nursing methods in the treatment of infectious diseases, such as compresses, poultice, wraps, baths⁶².
- f. Paediatrics: Knowledge on delayed or back up prescription should be provided to healthcare staff and patients.

Background: Delayed antibiotics are shown to be effective in reducing antibiotic use which children can especially benefit from with only minor health risks involved⁶³. E.g., a randomized clinical trial including 436 children with uncomplicated respiratory infection showed that there was no difference in the duration or severity between those that received either delayed or no antibiotic treatment compared to those that received immediate antibiotic prescription⁶⁴. In physicians' decision making, the patients' attitude also influences antibiotic prescription⁶⁵.

RESEARCH & DEVELOPMENT While the development of sustainable antibiotic R&D pipelines and innovation systems are crucial to ensure the effectiveness of existing and new antibiotics, increasing efforts should be put on testing non-antibiotic prevention and treatment strategies in clinical studies. Evaluation and research of Anthroposophic and Integrative Medicine approaches should be prioritized and supported, along knowledge being shared through appropriate tools.

- g. Identification and proof of best practices in Anthroposophic and Integrative Medicine with a focus on common diseases acute otitis media (AOM), acute respiratory tract infections (RTI), and skin infections⁶⁶ should be prioritized.
- h. Appropriate EU and international legislations and regulations for Anthroposophic and Integrative Medicinal products should be fostered.
- i. Outcomes of research should guide funding into research and to generate evidence in Integrative Medicine, as new therapeutic area.

https://www.who.int/healthpromotion/about/HPR%20Glossary%201998.pdf

⁶¹ World Health Organization, 1998: Health Promotion Glossary:

⁶² For further information visit: https://anthronursing.care/en/

⁶³ https://www.rcpch.ac.uk/resources/use-delayed-prescriptions-antibiotics-infants-children-statement

⁶⁴ Mas-Dalmau, G., Villanueva López, C., Gorrotxategi Gorrotxategi, P., et al. (2021). Delayed Antibiotic Prescription for Children With Respiratory Infections: A Randomized Trial. *Pediatrics*, *147*(3), e20201323: https://doi.org/10.1542/peds.2020-1323

⁶⁵ Raft, C. F., Bjerrum, L., Arpi, M., Jarløv, J. O., & Jensen, J. N. (2017). Delayed antibiotic prescription for upper respiratory tract infections in children under primary care: Physicians' views. *The European journal of general practice, 23*(1), 190–195: https://doi.org/10.1080/13814788.2017.1347628

⁶⁶ Based on 27,829 patient records, respiratory (52.1%), urinary (27.9%), and skin (4.8%) infections were the most common clinical indications for antibiotic prescribing. Martínez-González, N. A., Di Gangi, S., Pichierri, G., Neuner-Jehle, S., Senn, O., & Plate, A. (2020). Time Trends and Factors Associated with Antibiotic Prescribing in Swiss Primary Care (2008 to 2020). *Antibiotics*, 9(11): https://doi.org/10.3390/antibiotics9110837.

ONE HEALTH APPROACH⁶⁷ AMR should continue to be recognized and addressed as a multi-sectoral issue⁶⁸, in line with the EU environmental strategies and actions plans contributing to the objectives of the European Green Deal zero-pollution ambitions⁶⁹ and the European One Health Action Plan Against Antimicrobial Resistance⁷⁰, among other strategies.

Background: "To protect both public health and ecosystems, action is required throughout the whole lifecycle of medicines to reduce resource use, emissions and levels of pharmaceutical residues in the environment 71 . The overall exposure to such residues should be minimised and reduced as much as possible" 72 .

- j. European and international policies should promote the appropriate and prudent use of antimicrobials in all sectors, including human, animal and plant sectors to reduce the presence of AMR in the environment⁷³.
- k. European and international legislations on pharmaceutical manufacturing and supply chains should mitigate the environmental risk involved in the whole life cycle of pharmaceutical products⁷⁴.
- l. R&D of environmentally sustainable, safe pharmaceuticals to treat infectious diseases with low environmental risks should be promoted.
- m. Adoption of organic and biodynamic agricultural and animal husbandry approaches to reduce antibiotic use in animal husbandry should be supported in the EU and internationally⁷⁵. Background: "Enhanced animal welfare, hygiene conditions, and biosecurity on farms resulting from organic and biodynamic animal husbandry can help eliminate the need for preventive antibiotics contained in livestock feed and thus, reduce the likelihood of AMR in livestock and ultimately, the spread of resistance from animals to public health systems."⁷⁶

⁶⁷ "The production, use and disposal of medicines have environmental implications, as residues and waste products may enter the environment. Not only does this have a negative impact on the environment itself, some waste and residues may have endocrine-disrupting potential and others may increase the risk of antimicrobial resistance. The presence of antimicrobial pharmaceuticals in water and soil may play a role in accelerating the development of resistant bacteria." European Commission, 2020: Pharmaceutical Strategy for Europe: COM/2020/761 final, pp. 19.

⁶⁸ Thornber, K., & Pitchforth, E. (2021). Communicating antimicrobial resistance: the need to go beyond human health. *JAC-Antimicrobial Resistance*, *3*(3): https://doi.org/10.1093/jacamr/dlab096

⁶⁹ European Commission, 2019: The European Green Deal. <u>COM/2019/640 final.</u> Also see: European Commission, 2021: Pathway to a Healthy Planet for All EU Action Plan: 'Towards Zero Pollution for Air, Water and Soil': <u>COM/2021/400 final</u>

 $^{^{70}}$ The European Commission's One Health Action Plan against AMR calls for effective action against the AMR threat with the concern of the health not only humans, but also animals and the environment. One Health aims at addressing the issue of AMR with a concern to human, animal health and environmental suitability. European Commission, 2017

⁷¹ For reference see footnote nr. 69

 $^{^{72}}$ For reference see footnote nr. 67

⁷³ World Health Organization, December 16, 2020: Antimicrobial resistance, Report by the Director-General.

⁷⁴ For reference see footnote nr. 58

⁷⁵ Schwaiger, K., Schmied, E. M., & Bauer, J. (2010). Comparative analysis on antibiotic resistance characteristics of Listeria spp. and Enterococcus spp. isolated from laying hens and eggs in conventional and organic keeping systems in Bavaria, Germany. *Zoonoses and public health*, *57*(3), 171–180: https://doi.org/10.1111/j.1863-2378.2008.01229.x

Karreman, H.J. & Fulwider, W. (2015). Animal well-being on organic farms. Improving Animal Welfare: A Practical Approach: 2nd Edition. 267-277: https://www.researchgate.net/publication/282950443 Animal well-being on organic farms

⁷⁶ E.g., Österberg, J., Wingstrand, A., Nygaard Jensen, A., Kerouanton, A., Cibin, V., Barco, L., Denis, M., Aabo, S., & Bengtsson, B. (2016). Antibiotic Resistance in Escherichia coli from Pigs in Organic and Conventional Farming in Four European Countries. *PloS one*, *11*(6), e0157049: https://doi.org/10.1371/journal.pone.0157049



The international umbrella organization IVAA represents and coordinates the national anthroposophic doctors' associations from more than 30 countries. IVAA focuses on:

- Demonstrating the contribution of Anthroposophic Medicine to address major health challenges
- Obtaining formal recognition of Anthroposophic Medicine as an integrative medical system
- Advocating for registration and availability of anthroposophic medicinal products
- Advocating for access to anthroposophic treatments such as anthroposophic nursing, art therapies, eurythmy therapy and body therapies
- Promoting pluralism in medicine and the right of patients to access the treatment of their choice

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