

The increasing role of evidence-based phytotherapy in the treatment of CNS disorders

Max Zeller Söhne AG

PharmaSynergy, Paris, Salon Hoche | 12.09.2024 | Susanne Pass



Rising incidence of depression and anxiety



1990

Diseases of the respiratory tract	1
Gastrointestinal infections	2
Perinatal complications	3
Depression	4
Coronary heart diseases	5
Cerebrovascular diseases	6
Tuberculosis	7
Measles	8
Traffic accidents	9
Congenital deformities	10
Malaria	11
Chron.-obstr. lung diseases	12
Epilepsia	13
Iron deficiency anaemia	14
Protein deficiency symptom	15

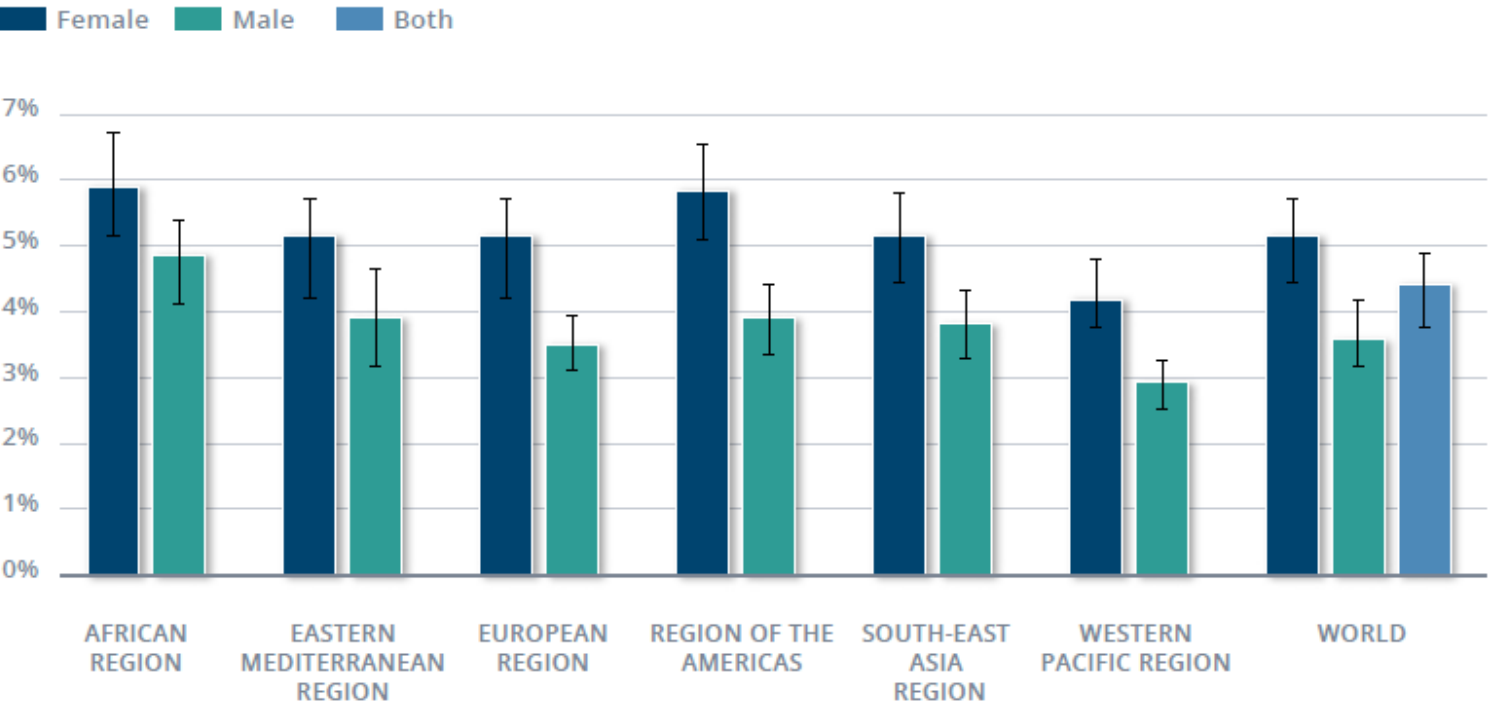
2030

1	Depression, anxiety disorders
2	Coronary heart disease
3	Traffic accidents
4	Cerebrovascular diseases
5	Chron.-obstr. lung diseases
6	Diseases of the respiratory tract
7	Tuberculosis
8	Effects of war
9	Gastrointestinal infections
10	HIV
11	Perinatal complications
12	Consequences of violence
13	Congenital deformities
14	Self-mutilation



Prevalence of depression

Prevalence of depressive disorders (% of population), by WHO Region

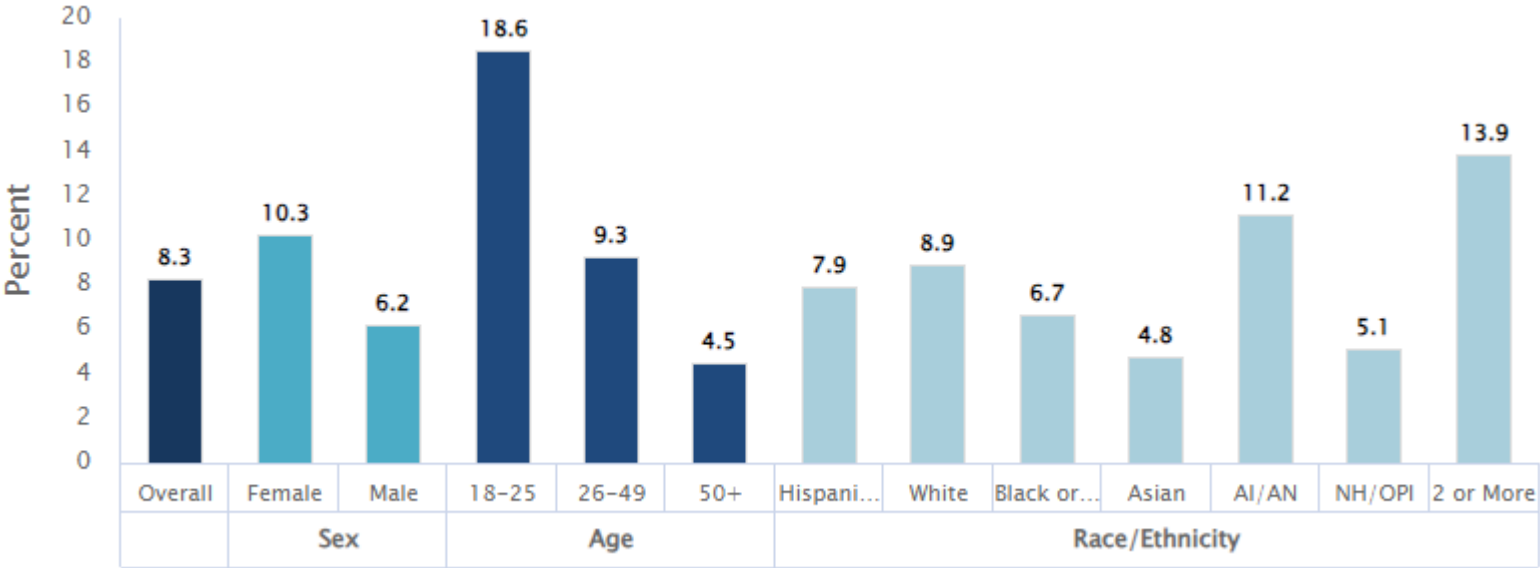


According to the World Health Organization (WHO), an estimated 322 million people are currently affected by depression. **This is equivalent to ca. 4.4% of the world**

Depression and other common mental disorders: Global health estimates. Geneva: World Health Organization. 2017.

<https://www.who.int/news-room/fact-sheets/detail/depression> (09.07.2024)

Prevalence of major depressive episodes among adults



The prevalence of adults with a major depressive episode was **highest among individuals aged 18-25 (18.6%)**

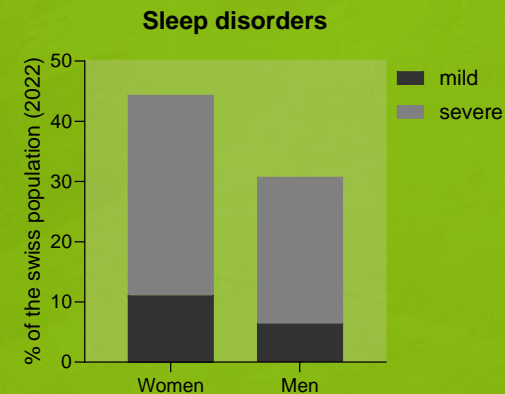
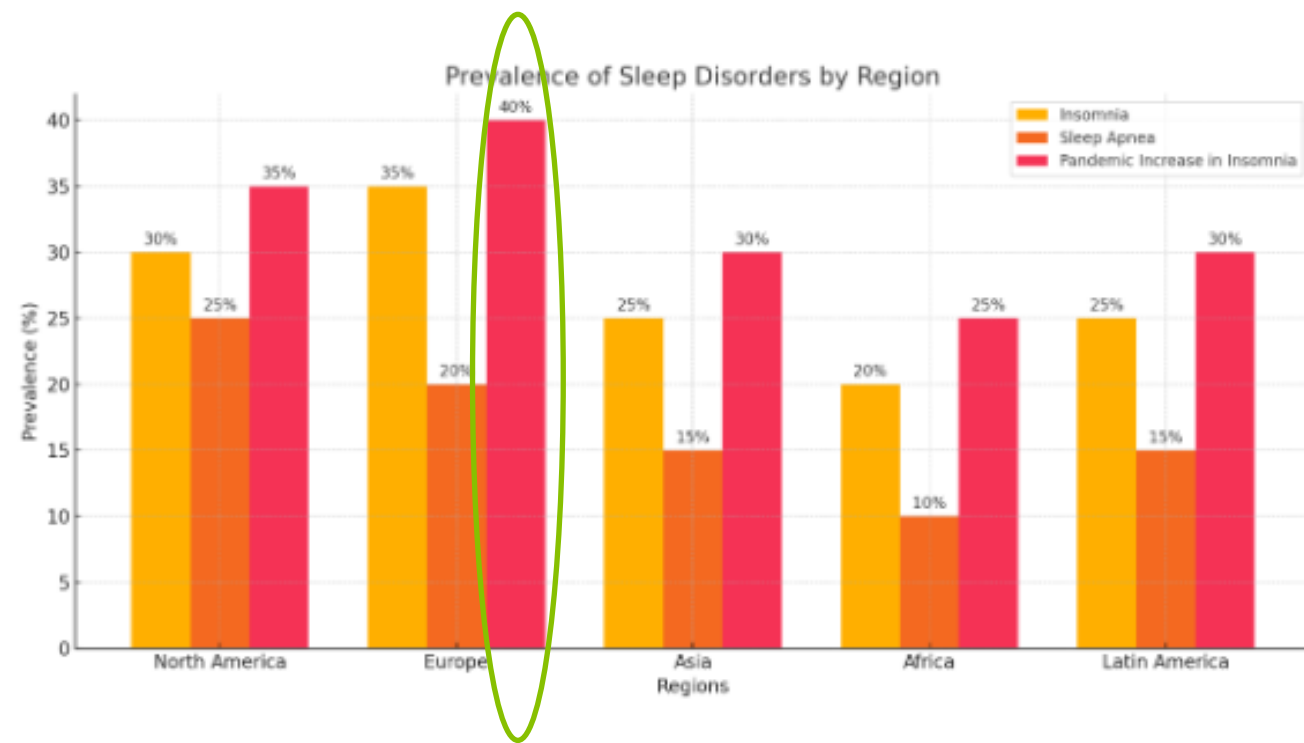
Prevalence of Major Depressive Episode Among Adults. National Institute of Mental Health. 2023.

Source: <https://www.nimh.nih.gov/health/statistics/major-depression>

Increasing prevalence of sleep disorders

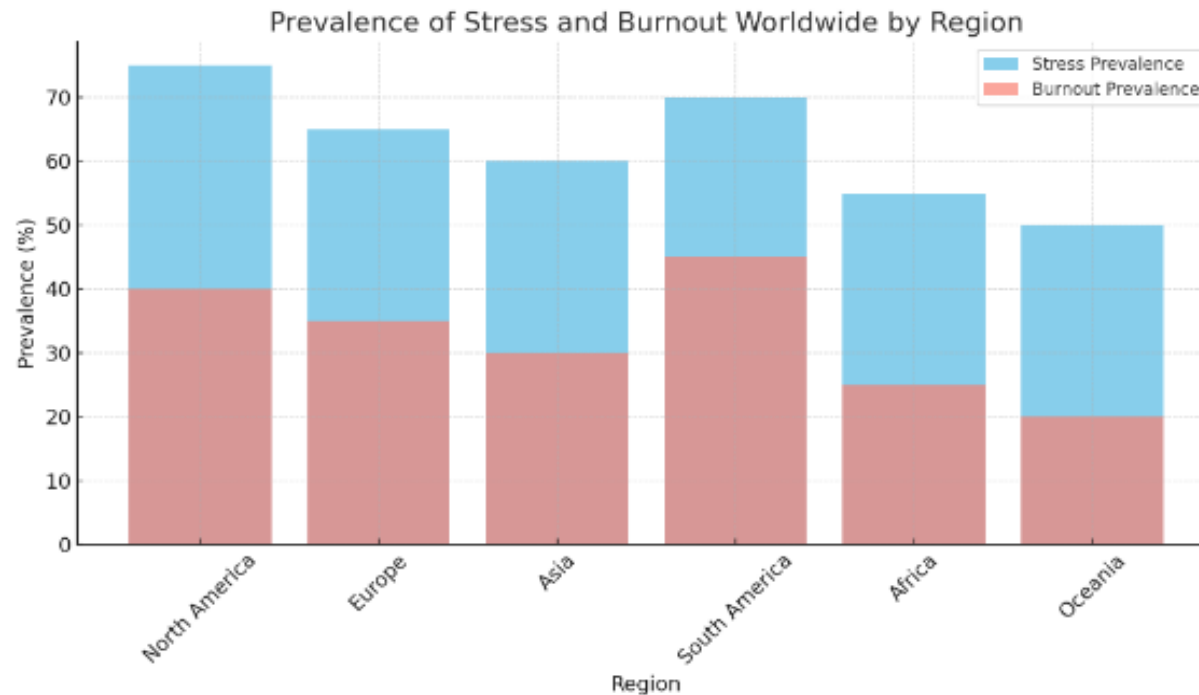
Prevalence of sleep disorders by region

- High increase in insomnia prevalence during the COVID-19 pandemic, rates of insomnia rose by 20-40%.
- 50% of elderly adults are suffering from sleep disturbances.
- More women are affected than man.



Source: Data from journals such as The Lancet Psychiatry and Sleep Medicine Reviews
Swiss Health Survey 2022; Swiss Confederation, Federal Statistical Office FSO (Schweizerische Eidgenossenschaft, Bundesamt für Statistik BFS)

Mental stress and burnout



About **60-70%** of the working age population show signs of stress

Mental Health Foundation. Stress: Are we coping?
London: Mental Health Foundation. 2018.

In both males and females, anxiety disorder is one of the most common mental disorders. In 2019, **301 million** people globally were living with anxiety disorders

World Health Organization. World mental health report: transforming mental health for all. 2022.

Adapted from different sources such as WHO, International labour organization and others

Switzerland has one of the highest numbers of
psychiatrists for its population in the world:
30 per 100'000 inhabitants

OECD „Health at a glance“ 2023

Antidepressants are the most frequently prescribed drugs in Switzerland

197 million daily
doses

9 million
inhabitants

More than 55 %
are SSRI

This is exactly where
Zeller steps in...

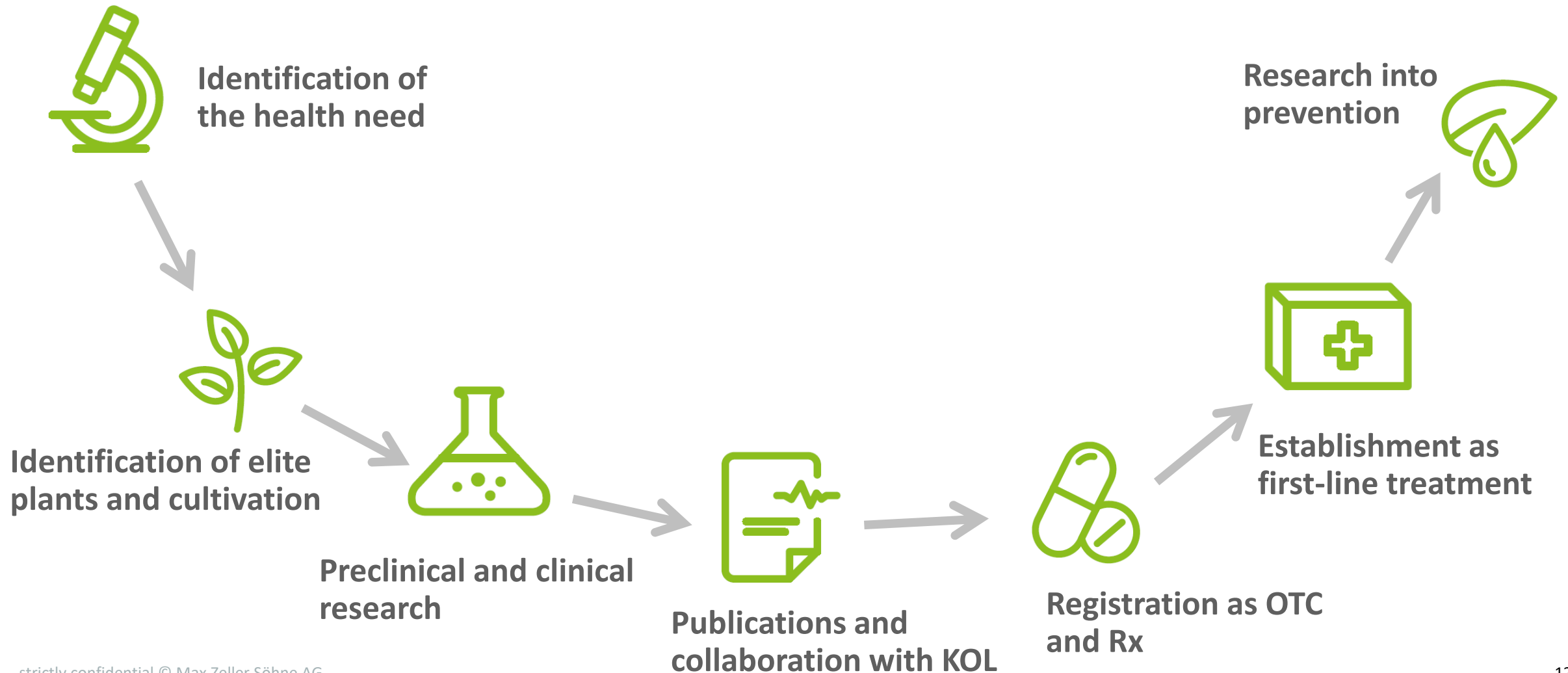


Zeller today

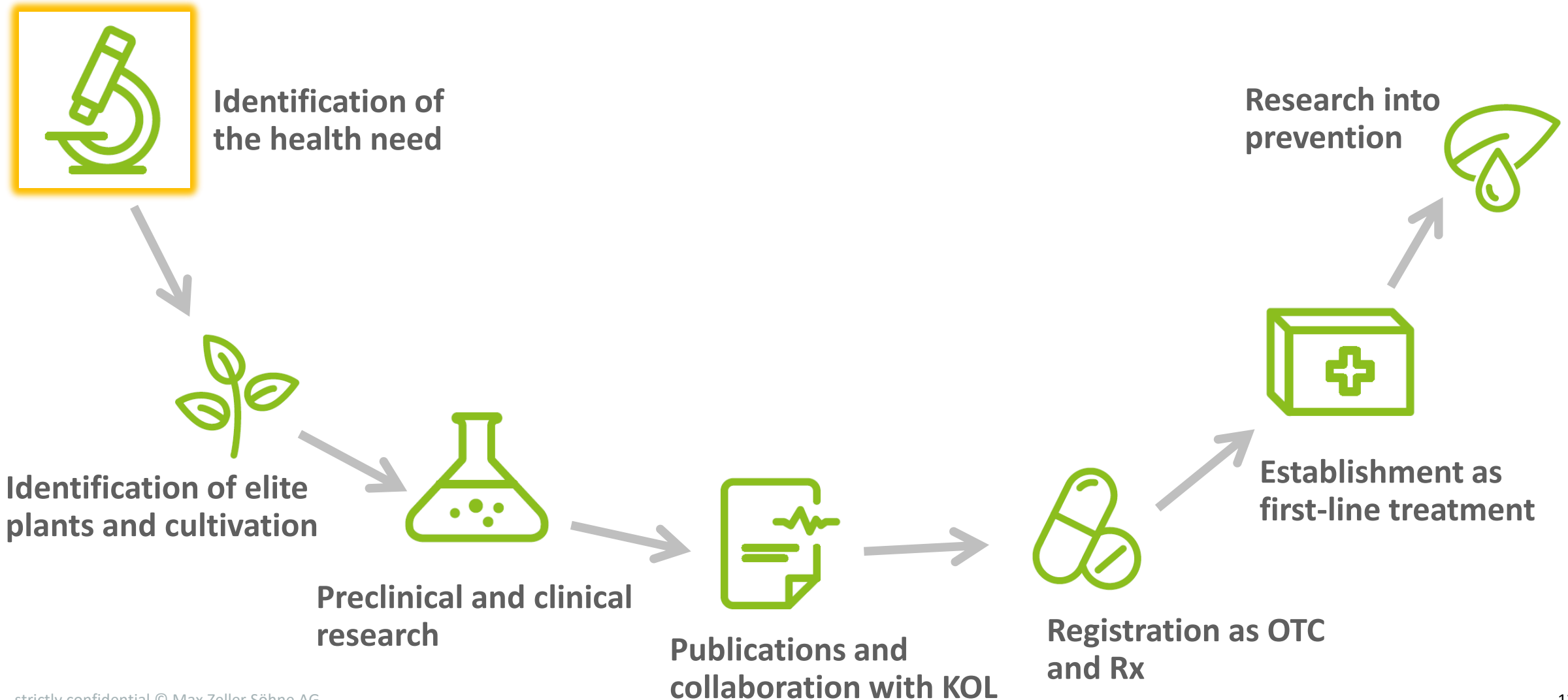
- ❑ Market leader in phyto-pharmaceuticals in Switzerland
- ❑ Family owned; now in the 5th generation
- ❑ 160 years of experience
- ❑ Focusing on CNS, women's health and allergy
- ❑ Employees: 160 in Switzerland and 200 in Kenya
- ❑ Zeller medicines available in more than 50 countries



From health need to sustainable treatment

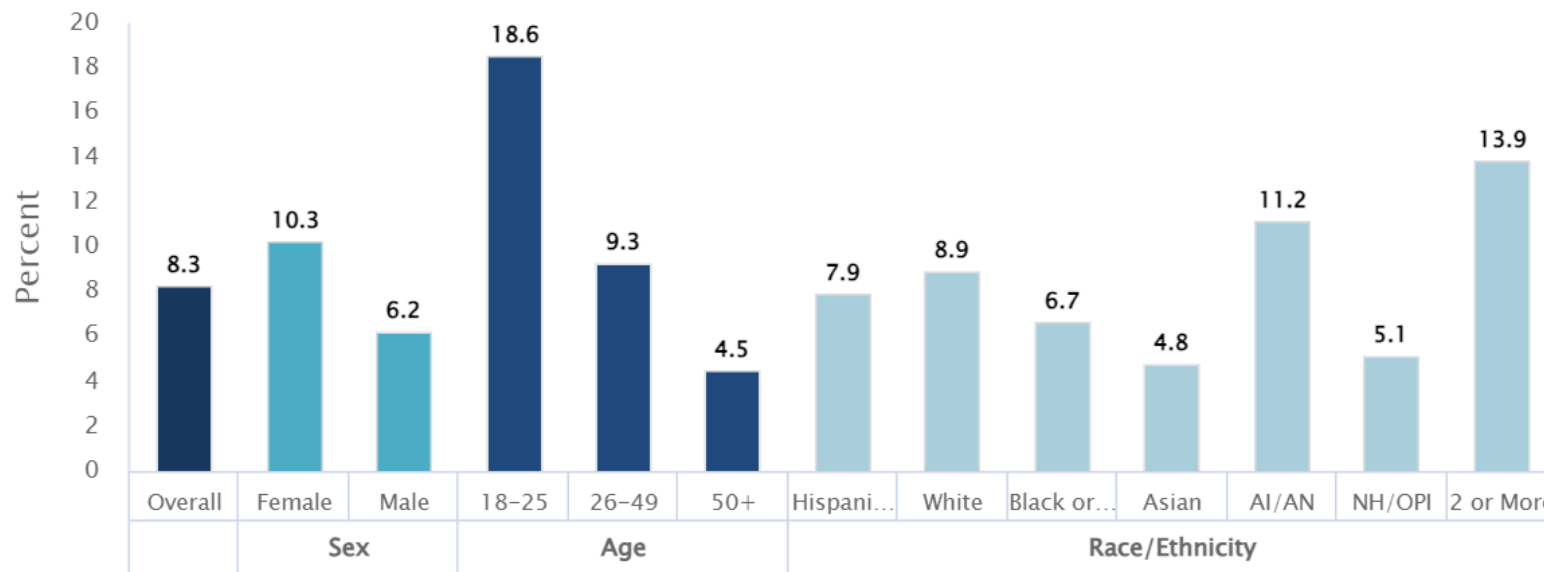


From health need to sustainable treatment





1) Identification of the health need

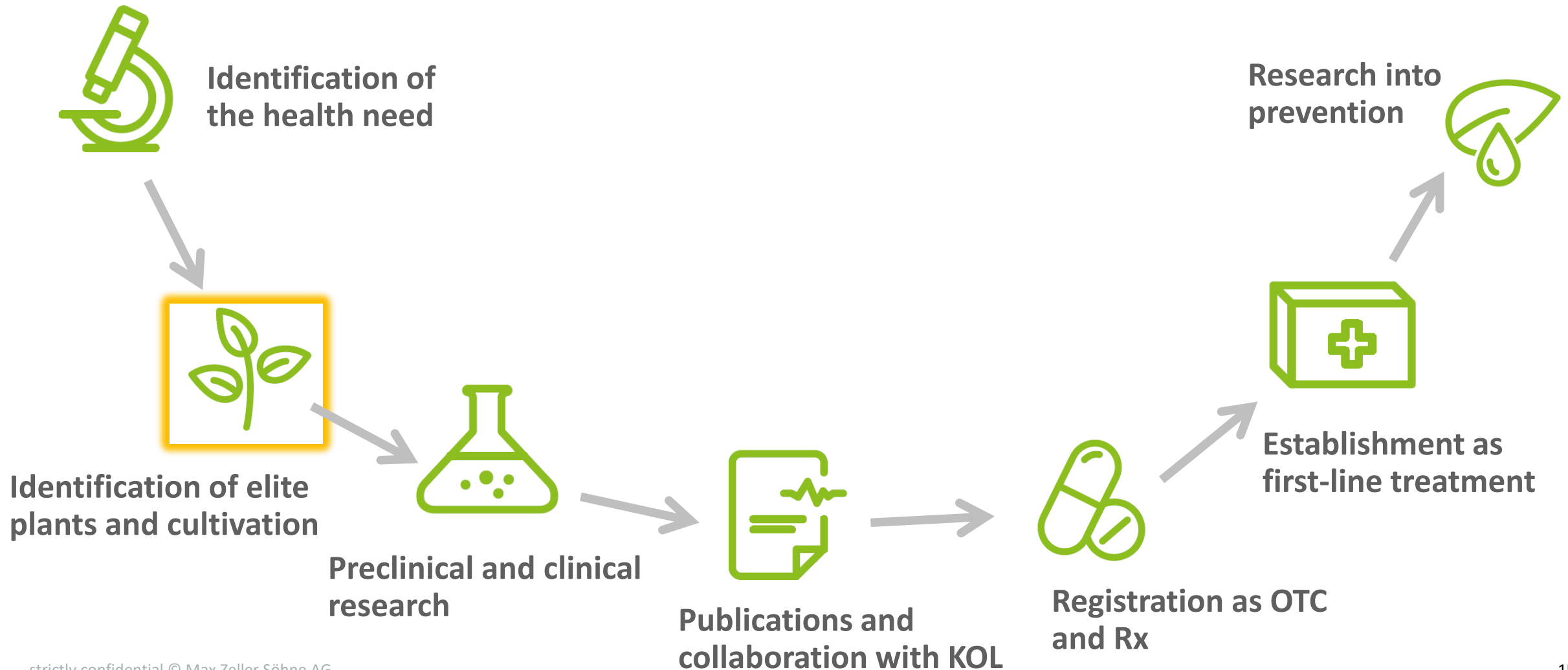


Target groups

- Patients with symptoms
- Patients with high comorbidity
- Younger adults
- Elderly people

Prevalence of Major Depressive Episode Among Adults. National Institute of Mental Health. 2023.

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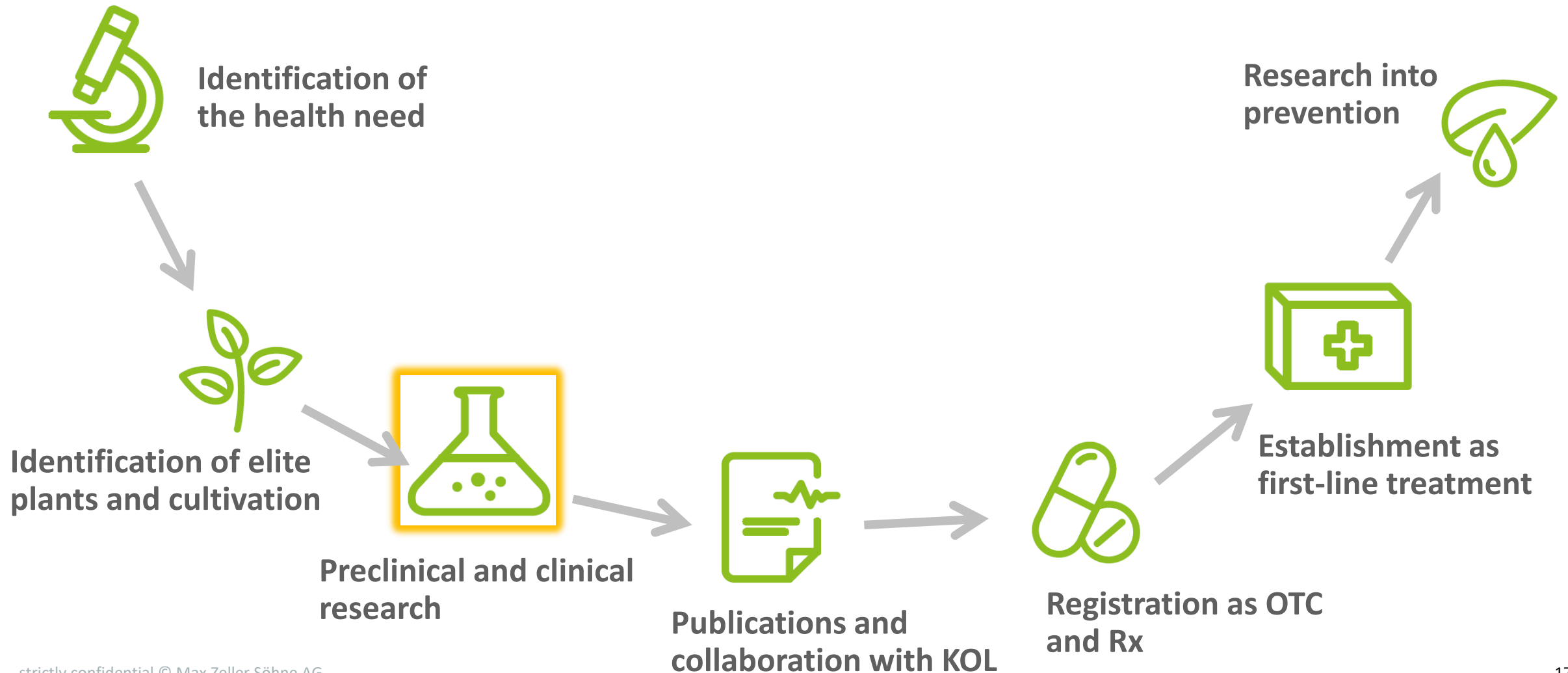


2) Identify elite plants

Plant species	Zeller protected variety
<i>Vitex agnus castus</i>	AGNUZELL
<i>Cimicifuga racemosa</i>	CIMIZELL
<i>Valeriana officinalis</i> L., radix	VIVAL
<i>Hypericum perforatum</i> L.	VITAN
<i>Petasites hybridus</i>	PETZELL

Development of protected plant varieties

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3) Preclinical and clinical research (Ze 117)

Proven clinical efficacy^{3,5-8}

Reduces HAMD score $\geq 40\%$ ^{3, 5-8}

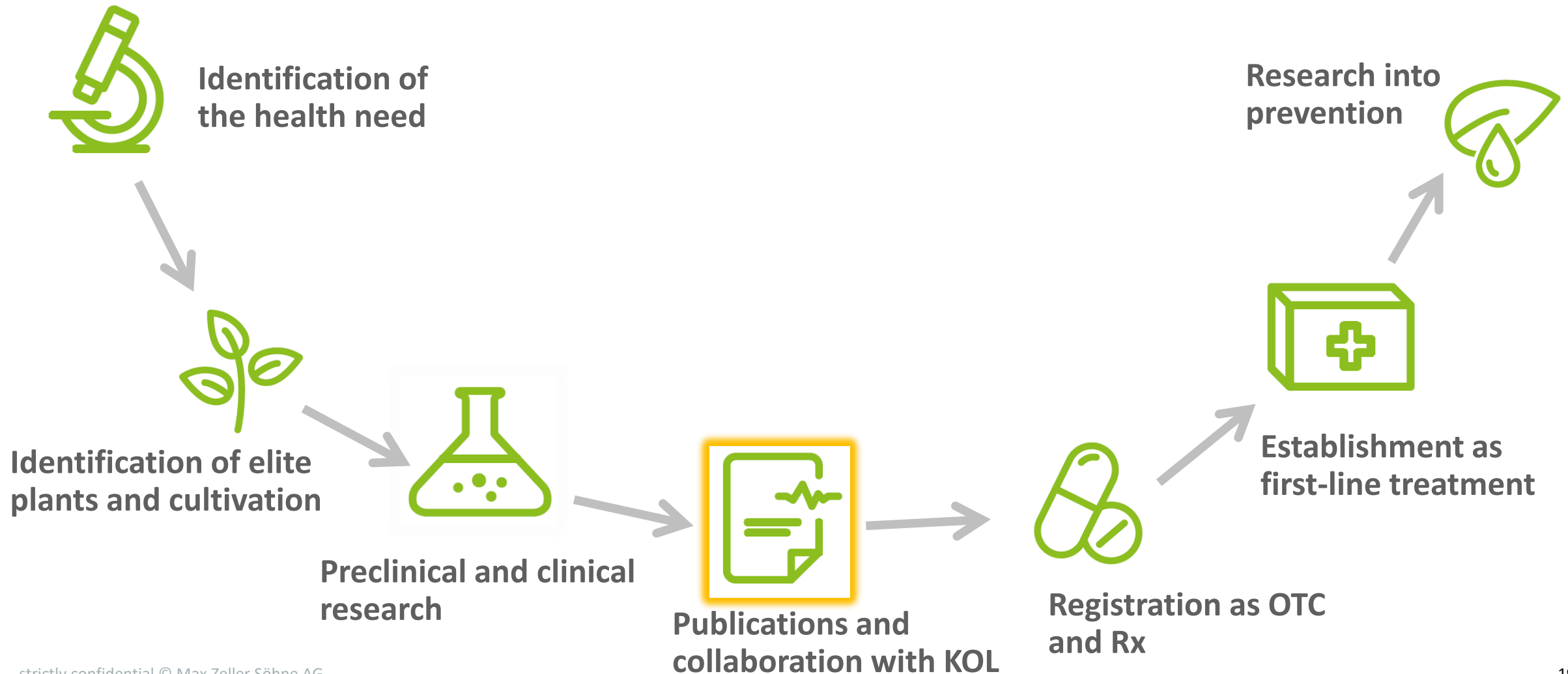
Non-inferiority to fluoxetine 20 mg/d
and imipramine 150mg/d^{5,6}

Low drug-drug interaction potential^{1,2,4}

60% less unwanted side effects compared to
fluoxetine⁶ and suitable for long-term use³

	Authors	Study endpoint	Methods	Results	Publication
1)	Zahner <i>et al.</i>	Safety of Ze 117: Pharmacokinetic interaction with 7 probe drugs	Open, single-sequence, phase I cocktail study in healthy volunteers	No clinically relevant interactions of Ze 117 were observed for CYP1A2, CYP2B6, CYP2D6, CYP2C9, CYP2C19, CYP3A4 and P-glycoprotein	Clin Pharmacol Ther (2019) 106(2):432-440
2)	Will-Shabab, L. <i>et al.</i>	Safety of Ze 117: Pharmacokinetic interaction with oral contraceptive	Open pharmacokinetic study in healthy volunteers	Ze 117 does not alter the pharmacokinetics of hormonal components of low dose oral contraceptive	Eur J Clin Pharmacol (2009) 65:287-294
3)	Brattström, A. <i>et al.</i>	Long-term safety and efficacy (1 year)	Open, multicentre safety study	Ze 117 is a safe and effective way to treat mild to moderate depression over long periods of time	Phytomedicine (2009) 16: 277-283
4)	Müller, SC. <i>et al.</i>	Safety of Ze 117: Pharmacokinetic interaction with digoxin	Randomized, placebocontrolled, parallel group pharmacokinetics study of digoxin	Ze 117 had no significant interaction with digoxin compared to hyperforinrich Hypericum extracts	Clin Pharmacol Ther (2004) 75: 546-557
5)	Woelk, H.	Ze 117 vs. Imipramine in mild to moderate depression	Prospective randomized, double-blind, parallel group controlled trial	Ze 117 is equivalent to imipramine in treating mild to moderate depression and better tolerated	British Medical Journal (2000) 321: 536-539
6)	Schrader, E. <i>et al.</i>	Efficacy and safety of Ze 117 vs. Fluoxetine in mild to moderate depression	Prospective randomized, double-blind, parallel grouped controlled study	Significant difference between Ze 117 and Placebo. 56% responders compared to 15% in placebo group after 6 weeks of treatment	Int Clin Psychopharmacol (2000), 15:61-68
7)	Schrader, E. <i>et al.</i>	Efficacy and tolerability of Ze 117 vs. placebo	Prospective, double-blind, randomized, placebocontrolled, multicentre study HAMD-21, CGI, VAS	Significant difference between Ze 117 and Placebo. 56% responders compared to 15% in placebo group after 6 weeks of treatment	Human Psychopharmacol 13: 163-169 (1998)
8)	Meier, B. <i>et al.</i>	Efficacy and tolerability	Observational multicenter study, HAMD	Reduction of 40 % of the initial value of depressive symptom score	Forsch Komplementärmed (1997) 4: 87-93

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4) Publications and collaboration with KOLs & universities

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Received: 10 July 2019 | Revised: 1 November 2019 | Accepted: 10 November 2019

DOI: 10.1111/bph.14936

REVIEW ARTICLE THEMED ISSUE



A reassessment of the clinical relevance of the drug interactions caused by St. John's wort

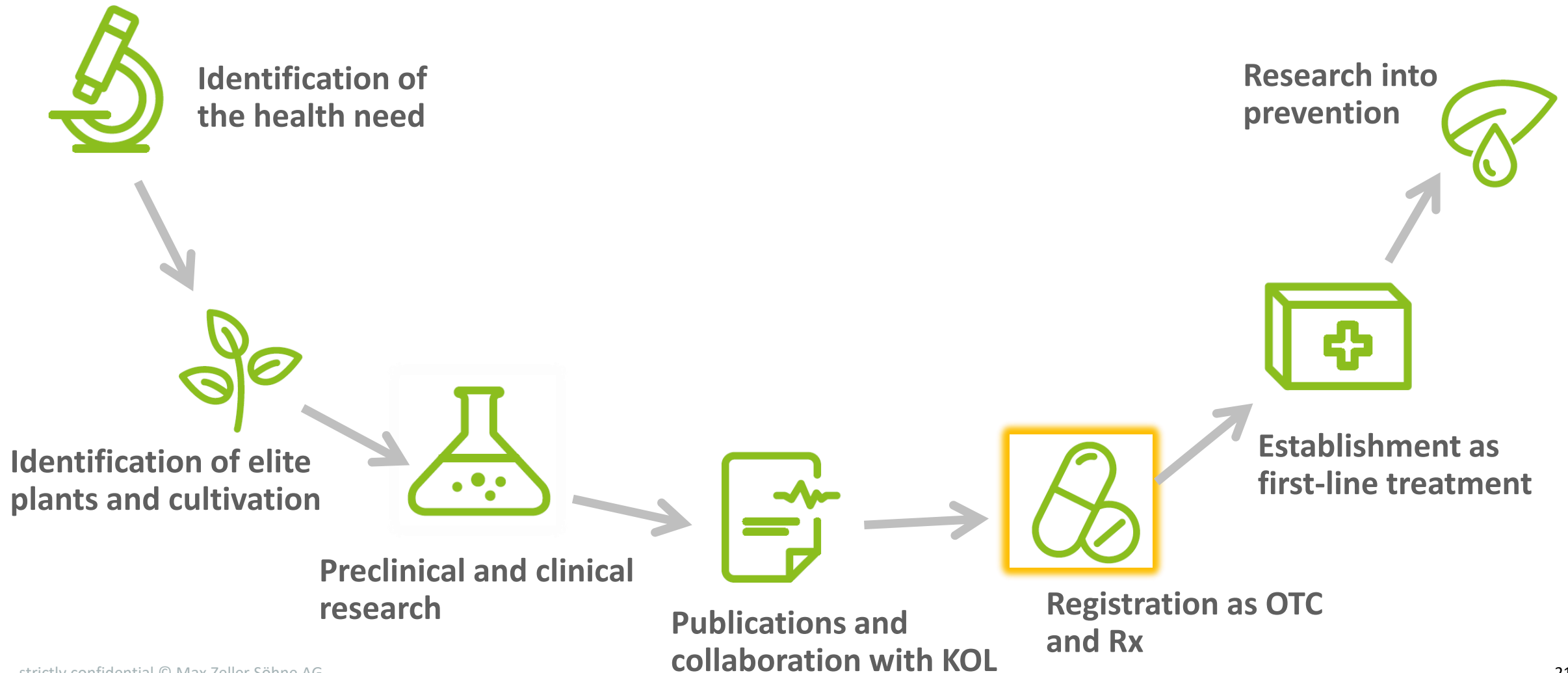
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The first clinically relevant reports of preparations of St. John's wort (SJW), a herbal medicine with anti-depressant effects, interacting with other drugs, altering their bio-availability and efficacy, were published about 20 years ago. In 2000, a pharmacokinetic interaction between SJW and cyclosporine caused acute rejection in two heart

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5) Registration as OTC and Rx

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**Evidence-based
treatments for:**



Sleep disorders

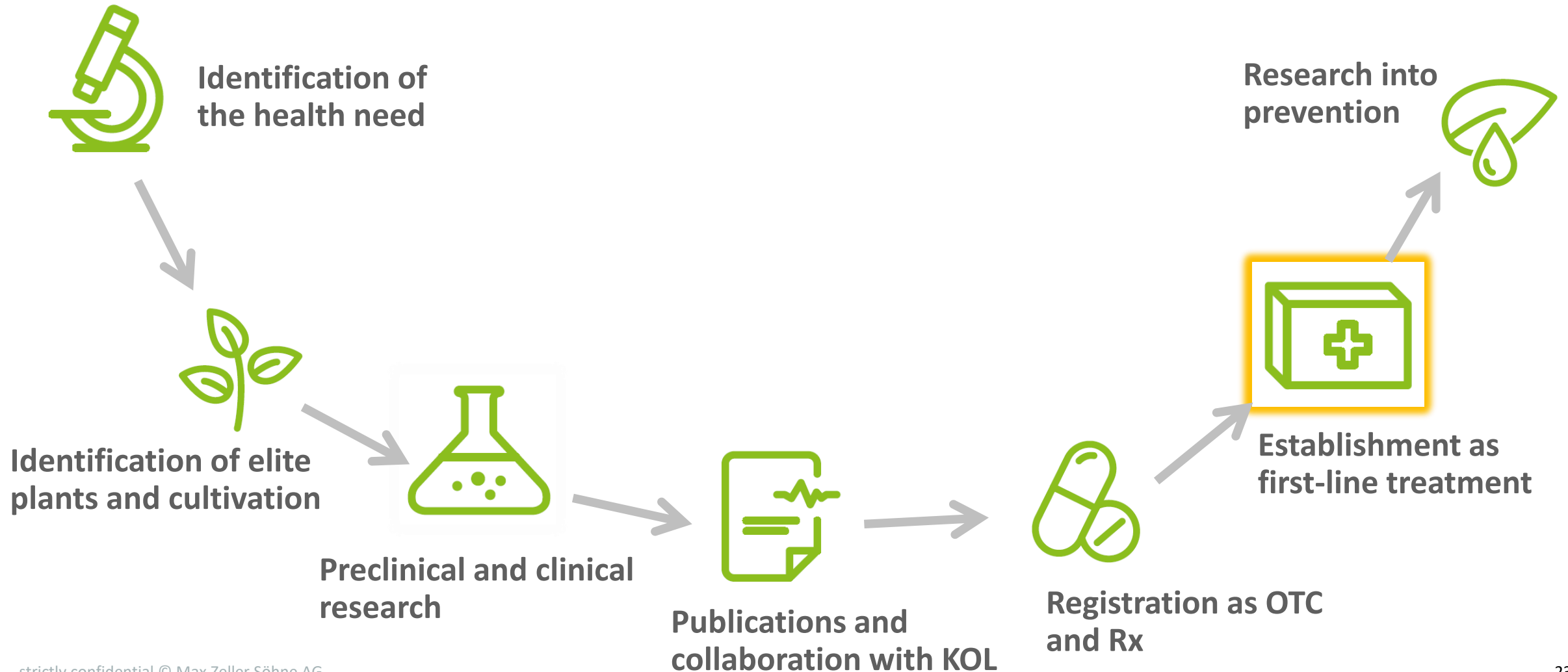


Depression



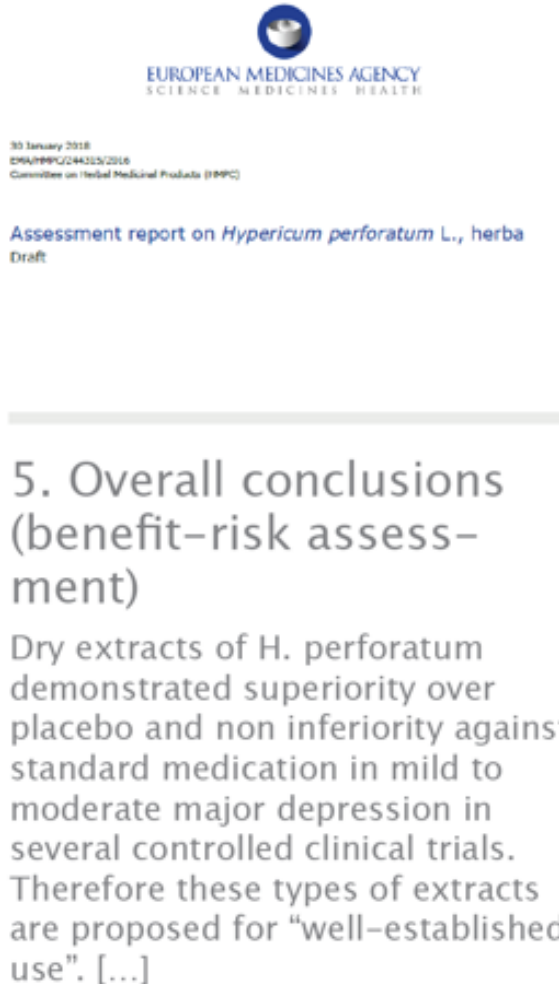
**Mental stress, anxiety,
nervousness**

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6) Established first-line treatment



St. John's Wort is recommended as

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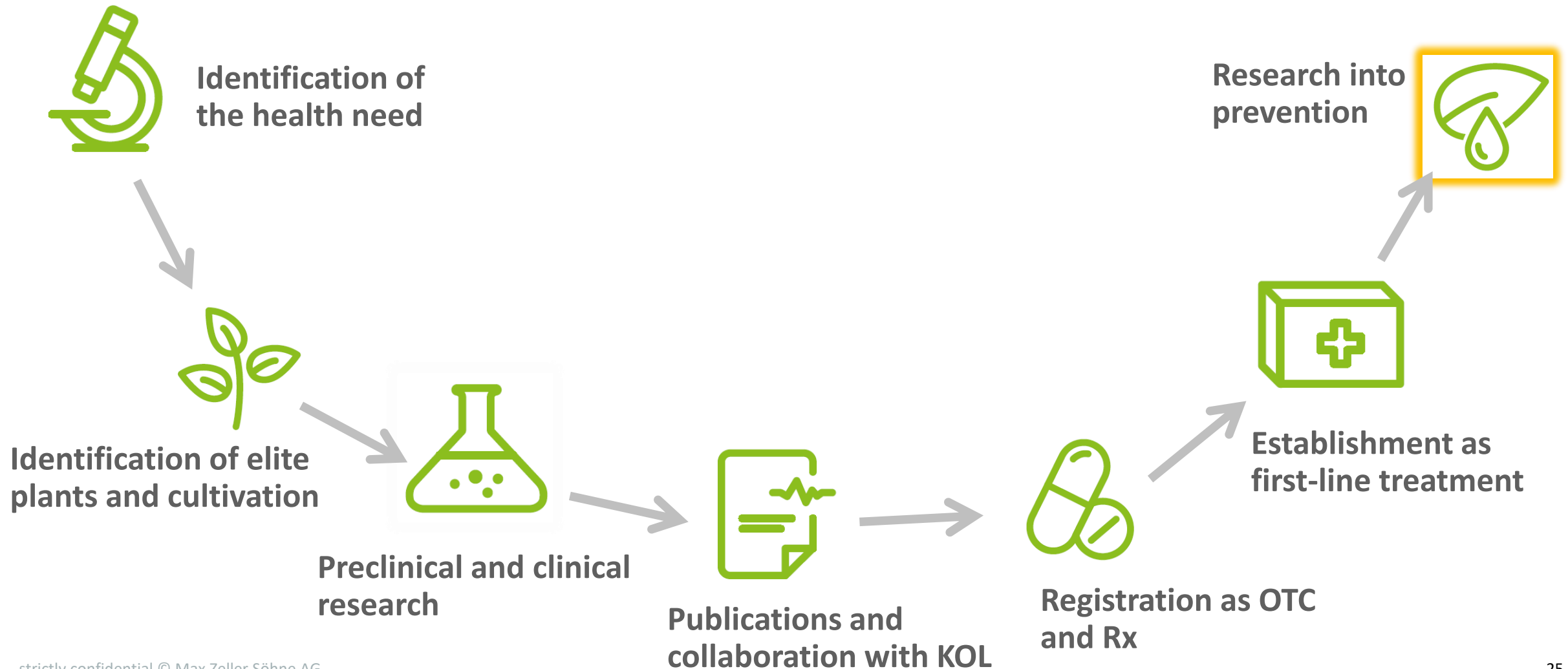
first-line treatment in international guidelines

“There is Level 1 evidence to support the **first-line use of St. John's wort as monotherapy in mild to moderate major depressive disorder**”, Canadian Network for Mood and Anxiety Treatment (CANMAT)

A.V. Ravindran et al. 2016 Can J Psychiatry 61 (9), 576-87 doi: 10.1177/0706743716660290.



From health need to sustainable treatment





7) Preventive phytotherapy

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**Ongoing research into
prevention of diseases**



From seed to health

From Switzerland to the world





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Thank you!

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