



---

# CML Patient Adherence Survey

CML Horizons, 4.5.2013, PRAGUE

GIORA SHARF

*Leukemia Patient Advocates Foundation*

# Non-adherence to TKI therapy has clinical implications

TKIs have revolutionised CML treatment so people can live longer

- The launch of imatinib, a BCR-ABL kinase inhibitor, transformed the treatment of CML, and indeed the face of oncology as a whole
- 2<sup>nd</sup> generation products, nilotinib and dasatinib, are designed to manage instances of imatinib resistance

However, non-adherence is a key issue in CML

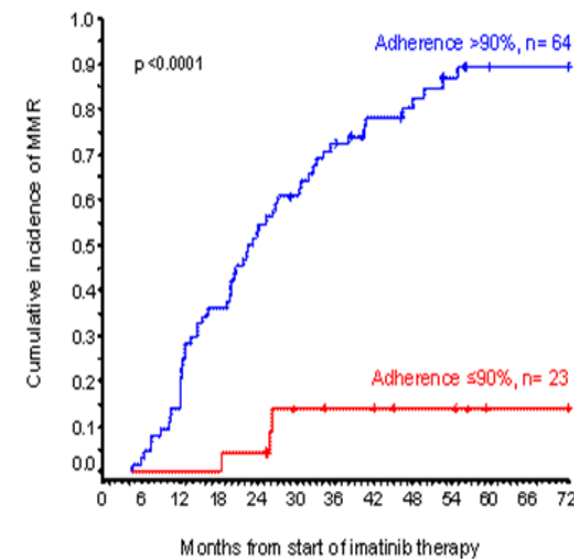
- Adherence is a complex and multifactorial issue, especially in medical conditions that require long-term therapy such as chronic phase CML
- A combination of internal and external factors may lead to reduced patient adherence to long-term therapies

There is a clear link between adherence and survival rates

- Both the HAMMERSMITH study and the ADAGIO study highlighted the importance of patient compliance in regards to achieving optimal treatment response
- Missing more than 2-3 daily doses each month can negatively impact response

## Long Term Adherence to Imatinib

Alex Bazeos et al, ASH 2009



# What we set out to explore

---

**The overall objective was to further understand the issue on non-adherence in CML, and investigate ways to maximise compliance and improve patient outcomes**



Provide greater understanding of patient behaviours associated with adherence, and help identify the 'true' issues behind non-adherence



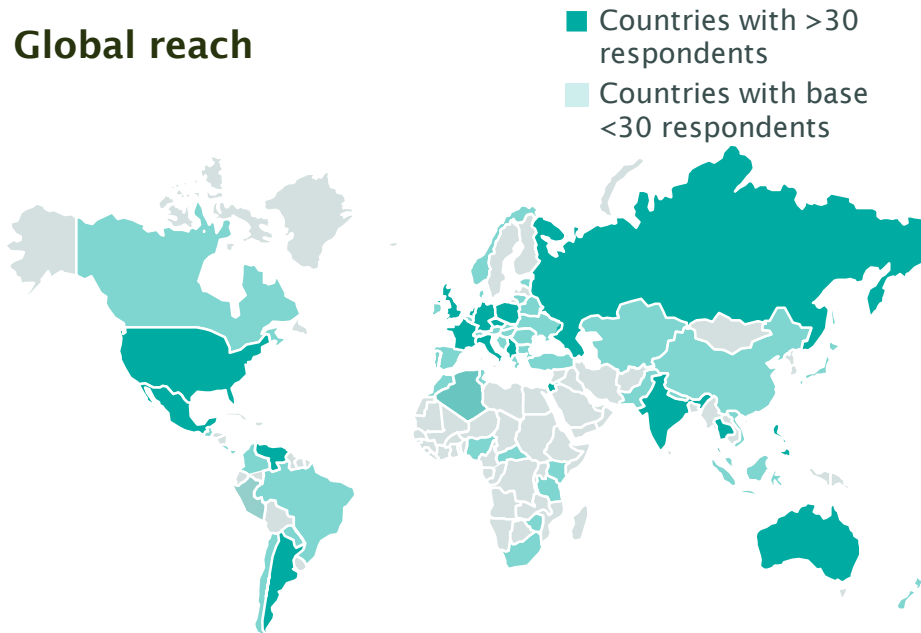
Explore the cultural influence and difference that exist with respect to patient concordance



Ultimately help to support development of physician and patient tools to improve compliance

# The research had truly global reach; an impressive number of respondents took part

## Global reach



## Sample: Total of 2546 respondents



## Methodology: Online and paper surveys

- Online - Recruited by patient associations via online forums & other methods
- **Many Patients groups did outstanding work to recruit their members**
- Paper & Pen (France, Germany, Italy) – Recruited by physicians at consultations
- Chronic Myeloid Leukaemia patients over 18 years old, currently taking oral medication for CML
- Fieldwork – 22<sup>nd</sup> September 2012 – 30<sup>th</sup> January 2013

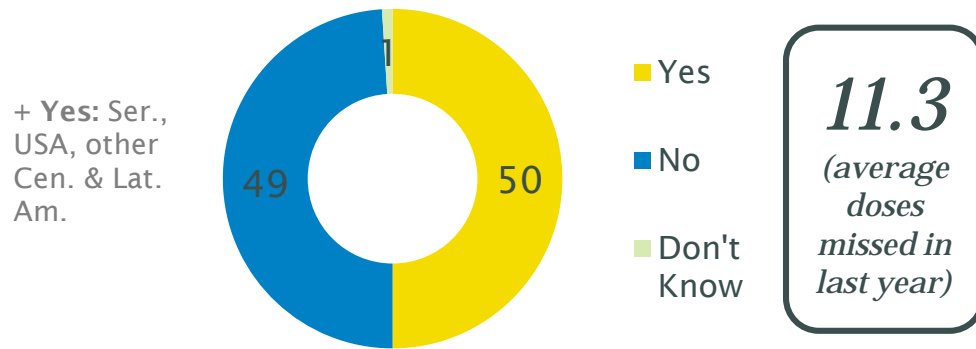


---

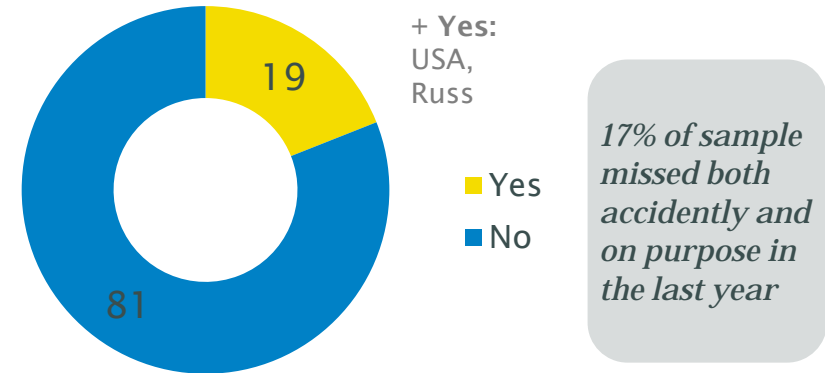
# Adherence Levels

# Half have missed a dose accidentally in the last year. 2 in 10 have decided to miss a dose

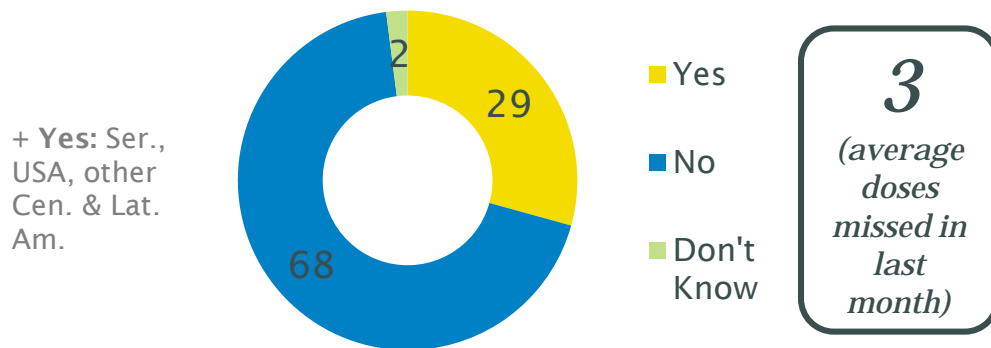
Missed a dose accidentally in last year %



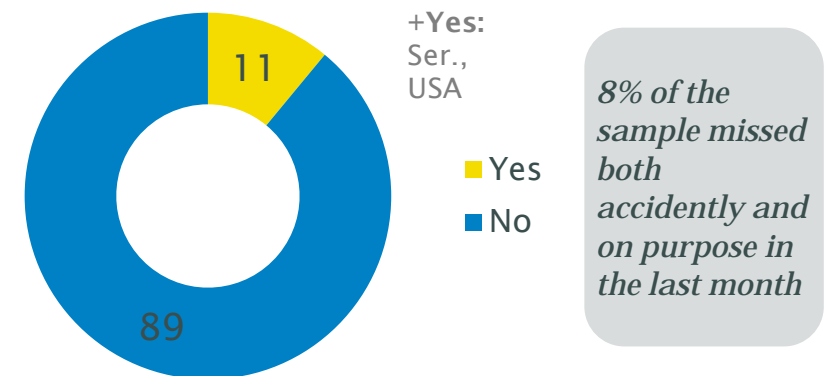
Decided to miss a dose in last year %



Missed a dose accidentally in last month %



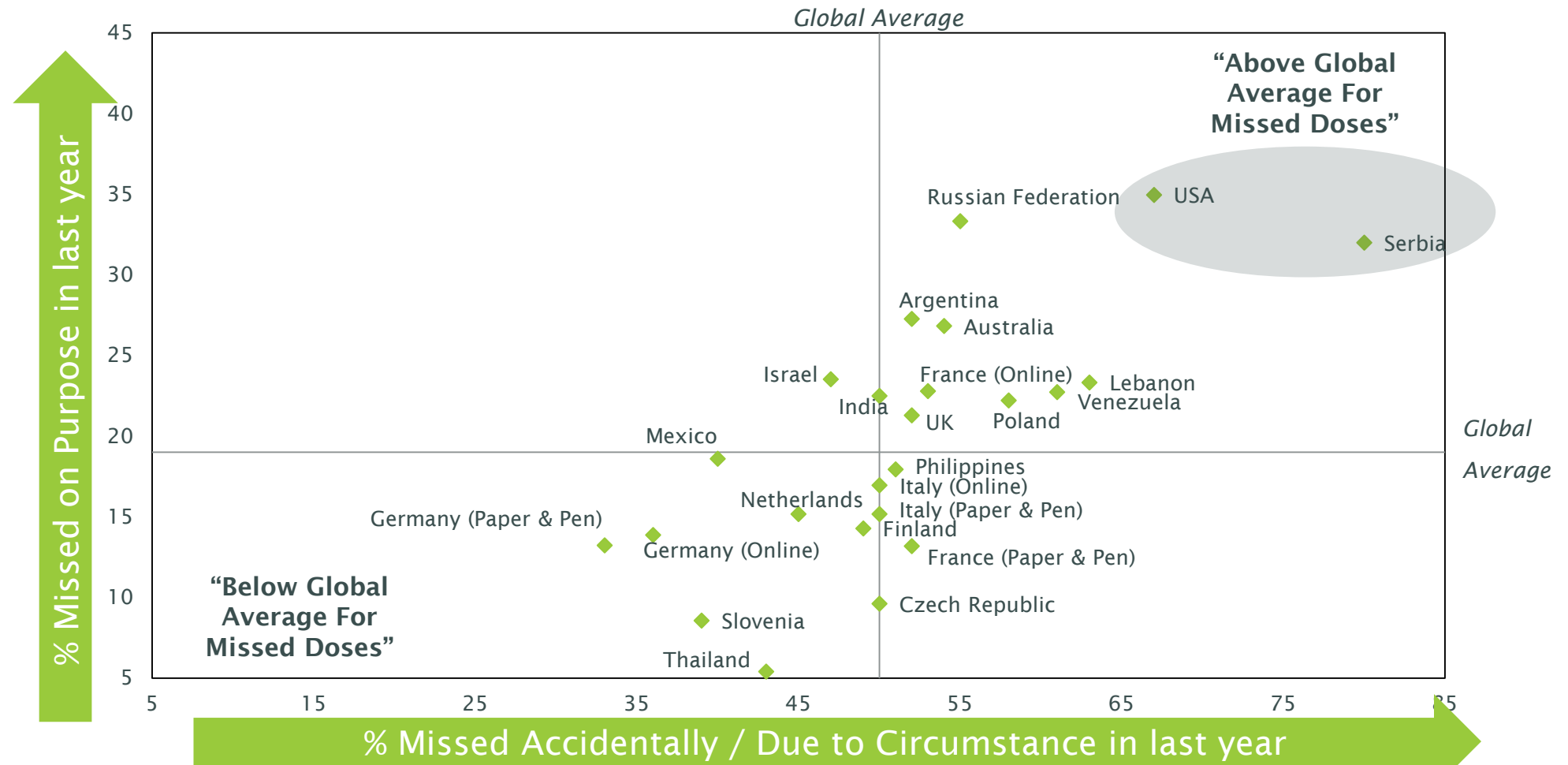
Decided to miss a dose in last month %



C2a / base=all respondents (n=2546) - Patients sometimes are not able to take their medication as prescribed. In the last month, have you missed a dose accidentally or due to circumstances that were outside of your control? C2b / n=746 How many doses did you miss in the last month? C2c / base=all respondents (n=2546) - In the last year, have you missed a dose accidentally or due to circumstances that were outside of your control? C2b & C2cc / base=all respondents (n=2546) - How many doses did you miss in the last month/year? C4a / base=all respondents (n=2546) - Patients sometimes make a conscious decision to miss a dose of medication. In the last month, have you decided to miss a dose? C4b / n=2258 - In the last year, have you decided to miss a dose?

# USA and Serbia stand out through the proportion missing doses, both accidentally & on purpose

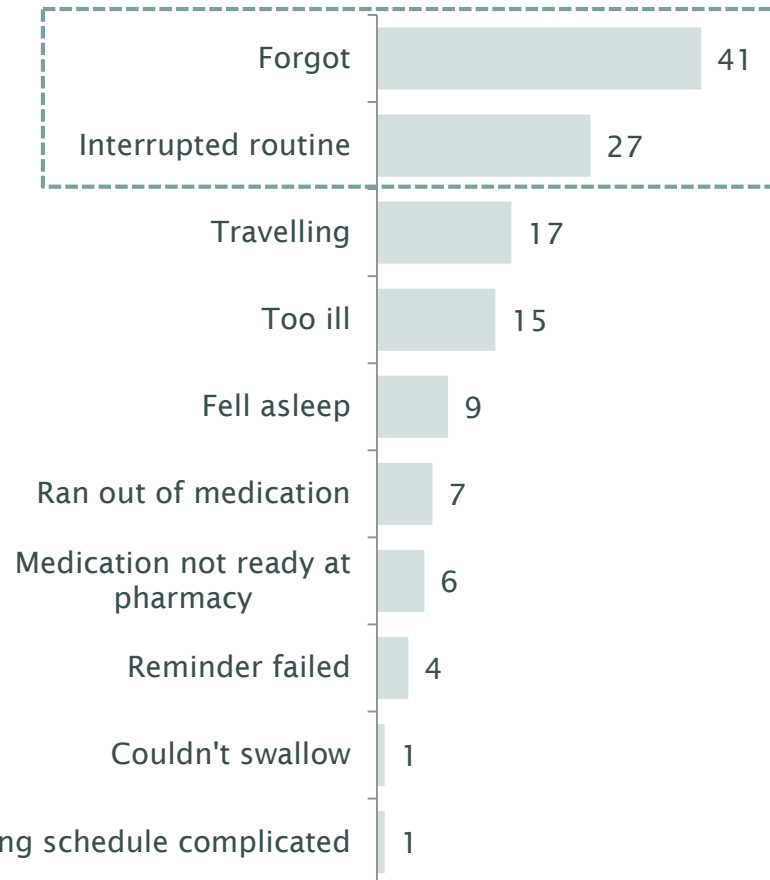
## Country Differences – Missed by accident / missed on purpose



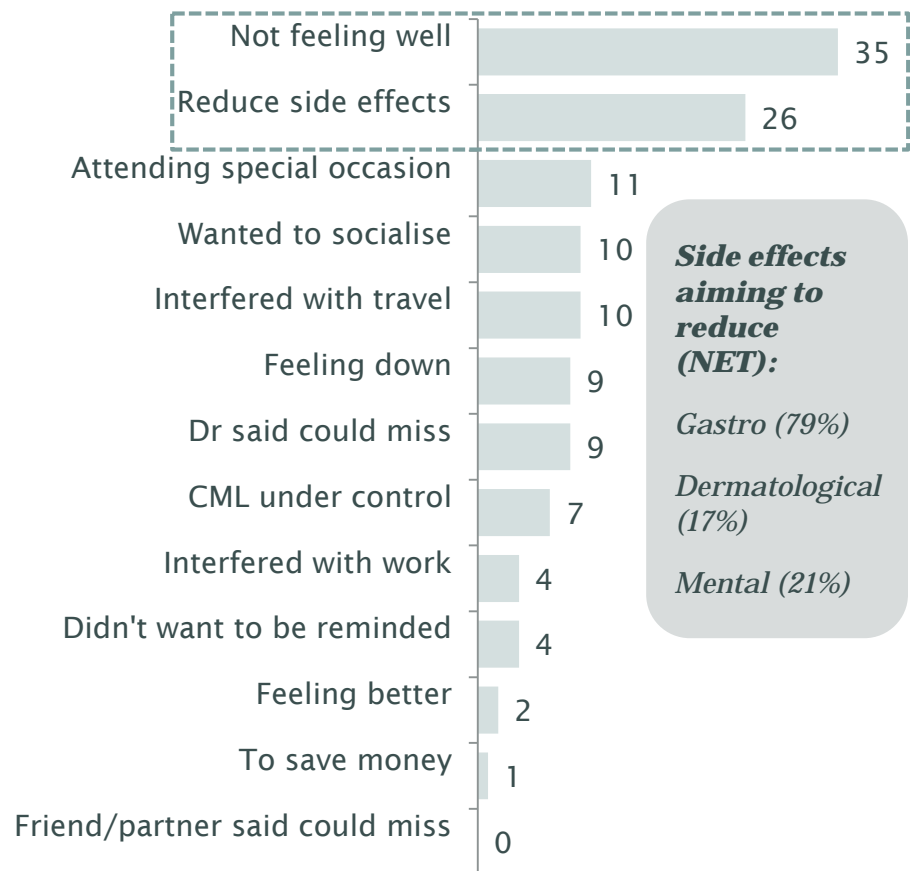
C2a / base=all respondents (n=2546) - Patients sometimes are not able to take their medication as prescribed. In the last month, have you missed a dose accidentally or due to circumstances that were outside of your control? C2c / base=all respondents (n=2546) - In the last year, have you missed a dose accidentally or due to circumstances that were outside of your control? C4a / base=all respondents (n=2546) - Patients sometimes make a conscious decision to miss a dose of medication. In the last month, have you decided to miss a dose? C4b / n=2258 - In the last year, have you decided to miss a dose?

# Forgetting & routine interruption are primary reasons for missing accidentally

Reason for missing accidentally % (n=1283)



Reason for deciding to miss % (n=491)



*Whilst accidental missing is more linked to memory, purposeful missing of doses is more related to physical symptoms*

C2d / n=1283 - Which circumstances led to a missed dose of your medication? C5 / n=491 - Why did you decide to miss a dose of your medication? C6 / n=126 - Which side effect(s) were you hoping to avoid by intentionally missing one or more doses of your medication?



*"It is possible that if I get distracted during my breakfast, I might forget to take the medication or I might think I already took it."*  
**Czech Republic**

*"No routine because I do not have any routine in my life. I get up at a different times every day and go to sleep at a different time. I go to the office at different times, eat breakfast, lunch and dinner at irregular times. My life is very messy and irregular and therefore I sometimes forget to take my medication.."*  
**Netherlands**

*"I wouldn't advise watching TV because if you're tired you may fall asleep and forget the last intake."*  
**Argentina**

*"I usually take them in the morning and at midday, the rare occasions when I forget, I take them in the evening."*  
**Italy**

*"Everything is simple, I don't know any patient who wouldn't remember about his own disease. However, there might be occasions when I forget, but it is very rare, so I simply know that I have to take the medication at a set time."*  
**Kazakhstan**

## On forgetting

Base: All Respondents (n=2546). E3 Do you have any suggestions for tools or routines that could help patients remember to take their CML medication? Please include routines that you use for taking your CML medication. (Open End Response)

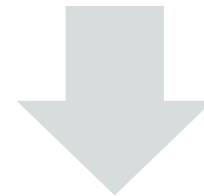
# About ¾ of respondents believe they take their CML medication exactly as prescribed – but they don't.

## Self rated adherence (rated 1-5) %

■ 1 - Rarely take exactly as prescribed ■ 2 ■ 3 ■ 4 ■ 5 - Always take exactly as prescribed



+ Neth., Slov.,  
Thai., It.  
(paper)



*However, 19% of those who stated 'I always take my medicine exactly as prescribed' had missed a dose accidentally in the last month. This indicates that there may be a gap between perception & reality for some.*

C1 / base=all respondents (n=2546) - In general, to what extent do you think you are able to stick to your CML therapy schedules and dosage, as prescribed by your CML doctor? C1 / C2a / base (n=1886) - Patients sometimes are not able to take their medication as prescribed. In the last month, have you missed a dose accidentally or due to circumstances that were outside of your control?

# We also used the Morisky Adherence Scale as a validated measure of adherence

Respondents answer a variety of questions about their adherence

## Forget medication

1. Do you sometimes forget to take your CML pills?

## Miss for other reason

2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your CML medicine?

## Stopped because felt worse

3. Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?

## Forget when travelling

4. When you travel or leave home, do you sometimes forget to bring along your CML medication?

## Take yesterday?

5. Did you take your CML medicine yesterday?

## Stop when under control

6. When you feel like your CML is under control, do you sometimes stop taking your medicine?

## Inconvenience

7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your CML treatment plan?

## How often difficulty remembering

8. How often do you have difficulty remembering to take all your medications?

- Never or rarely / once in a while / sometimes / usually / all the time

Based on respondent answers, an algorithm is used to calculate an adherence score. Respondents are then classified into different adherence groups :

Low



Medium

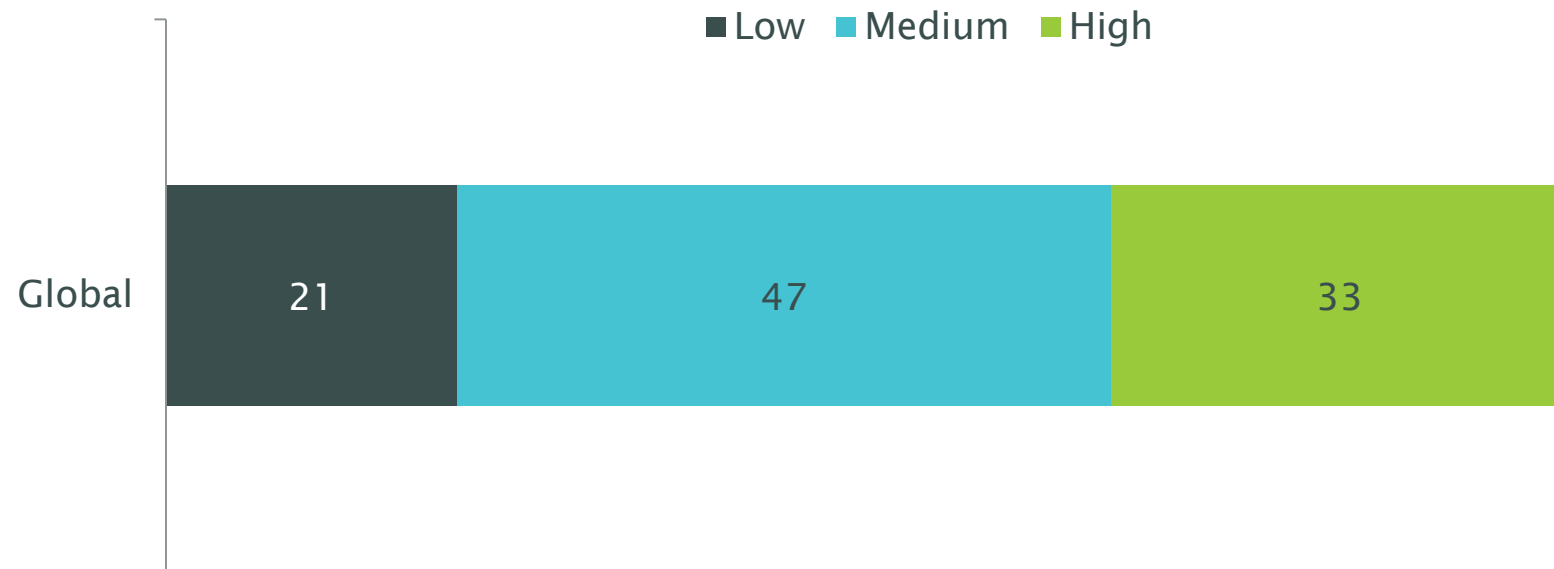


High



# According to the Moriskey scale, one fifth of respondents qualify as having “low” adherence

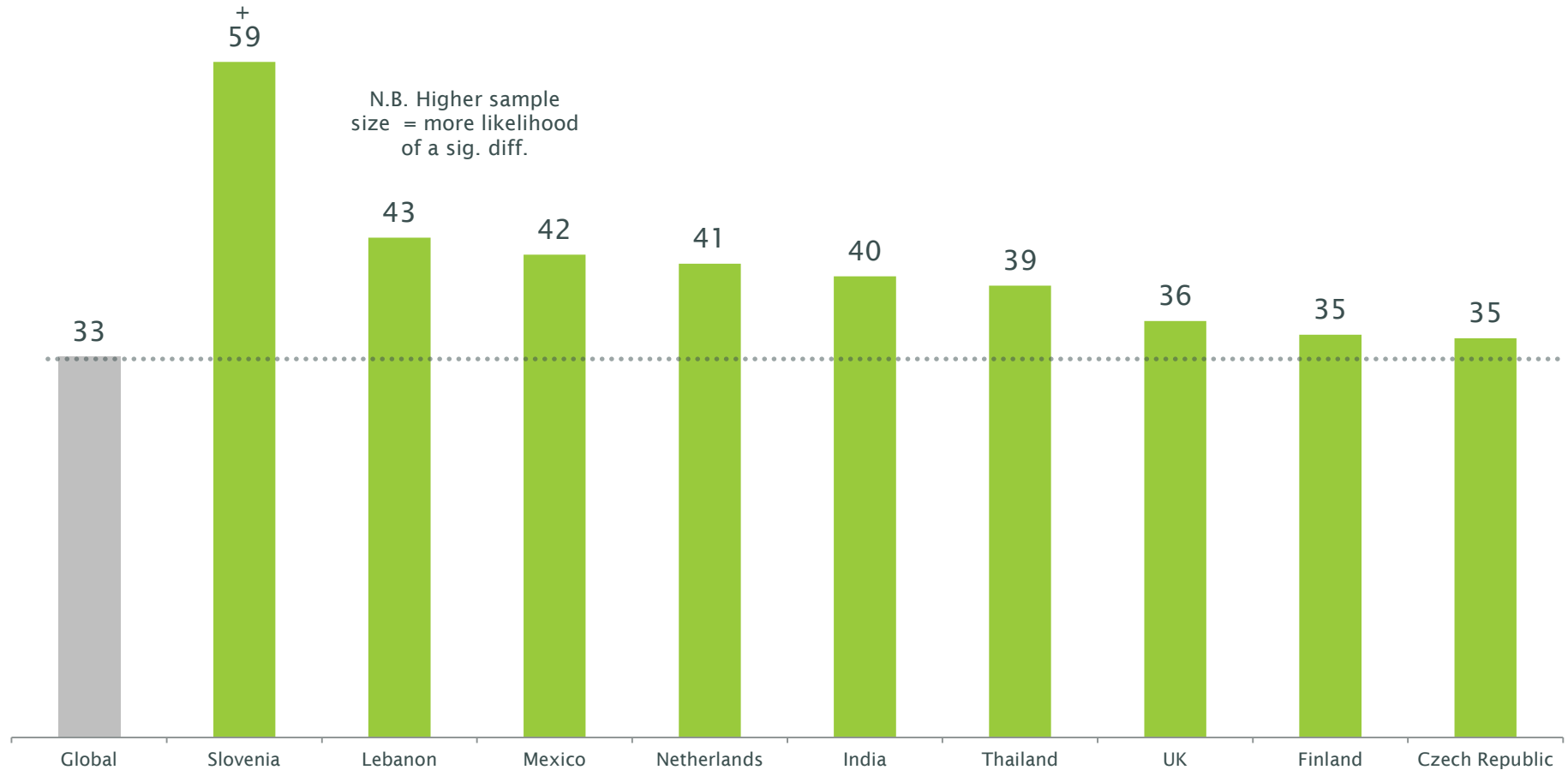
## Global adherence %



F1/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - Please answer 'yes' or 'no' to each question based on your personal experience with your CML medication. F2/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How often do you have difficulty remembering to take all your medications?

# Slovenia stands out as the most adherent country via the Morisky scale

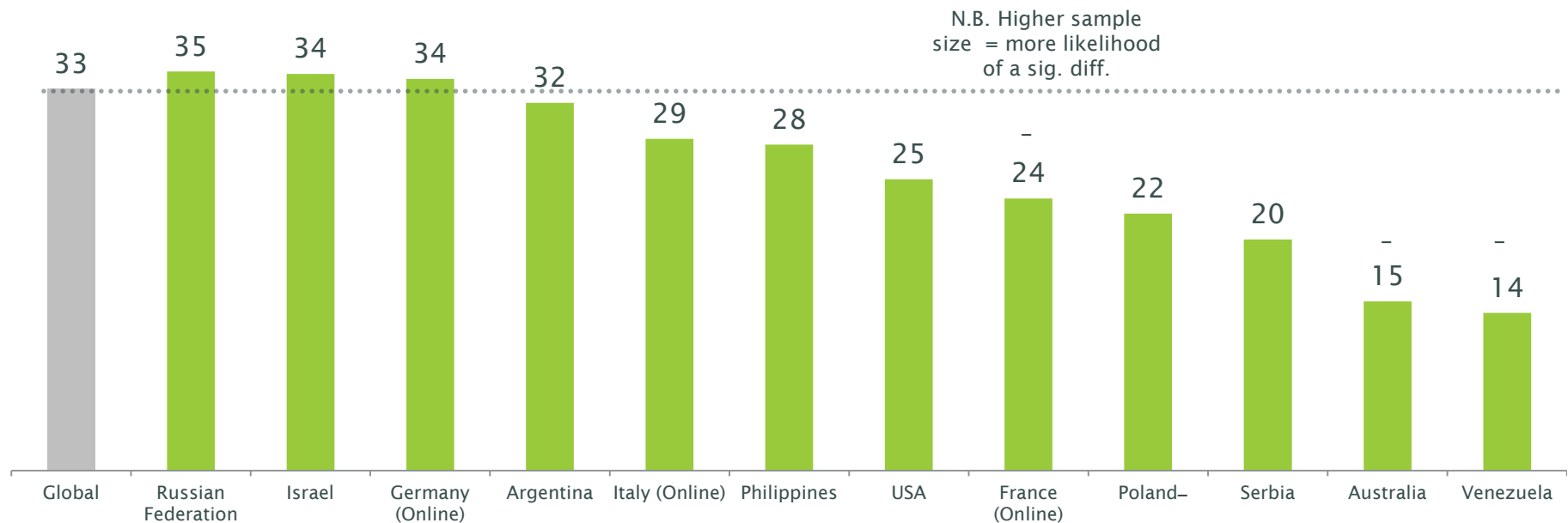
## Adherence by Market - Proportion Classified as High %



F1/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - Please answer 'yes' or 'no' to each question based on your personal experience with your CML medication. F2/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How often do you have difficulty remembering to take all your medications?

# Venezuela & Australia have the lowest proportion of adherent patients according to the Morisky scale

## Adherence by Market - Proportion Classified as High %



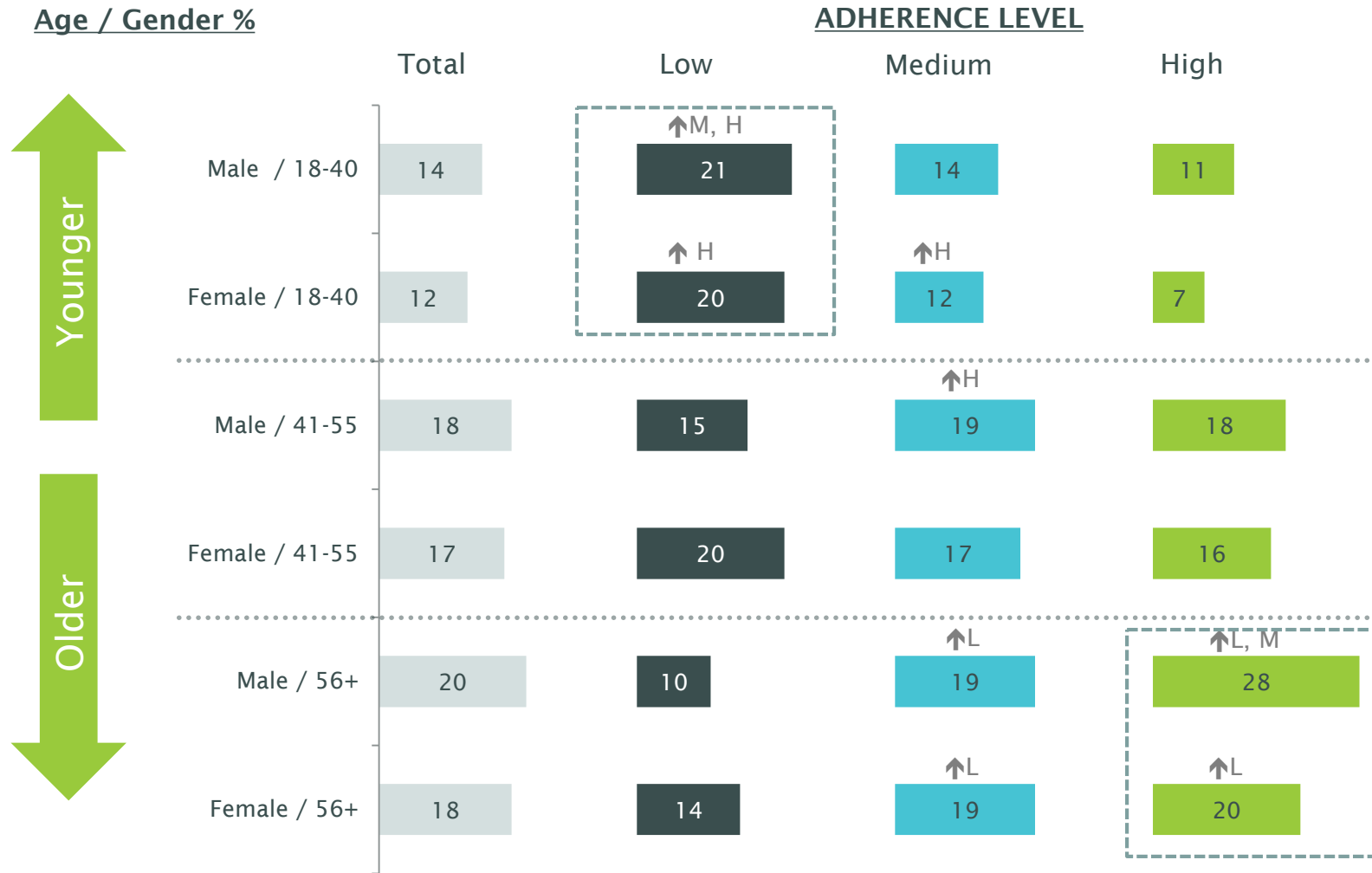
F1/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - Please answer 'yes' or 'no' to each question based on your personal experience with your CML medication. F2/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How often do you have difficulty remembering to take all your medications?



# Demographics & Treatment



# Those within the low adherence group have a younger age profile vs. the other groups

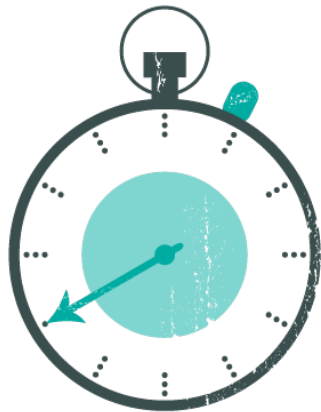


A1 / base=all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How old are you? A2 / base=all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - What is your gender?



# Those in the lower adherence group are more likely to have lived with the disease for longer

## Time since diagnosis (Av. Years)



*Total*  
**5.4**



↑ H, M  
*Low*  
**5.8**



*Medium*  
**5.2**



*High*  
**5.3**

+Ind., USA,  
Ven., Fr.  
(Paper)

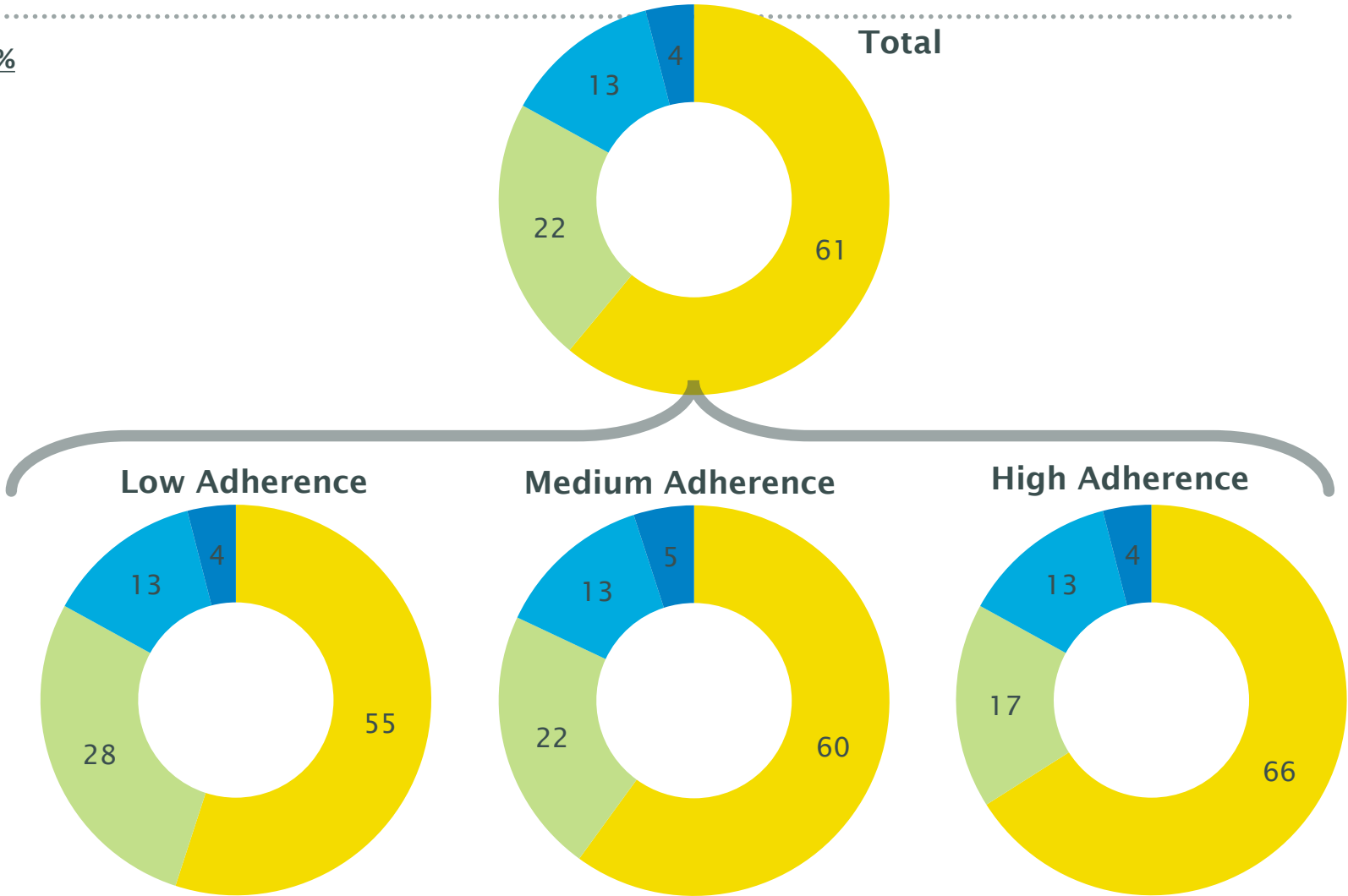
*High adherers (12%) are significantly more likely to be diagnosed less than a year ago than those in the low (5%) adherence group*

B2 / base=all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - When were you diagnosed with CML?

# Imatinib seems to be linked with higher adherence, Nilotinib is more prevalent in the low adherence group

Current Medication %

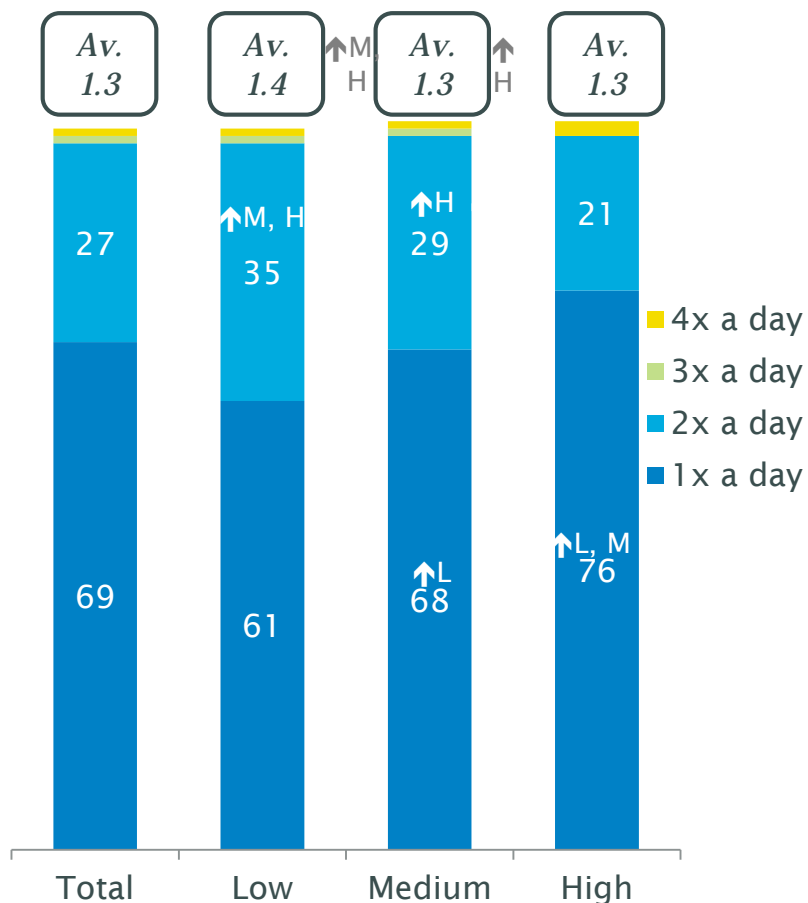
- Imatinib
- Nilotinib
- Dasatinib
- Other (inc. ponatinib) + don't know



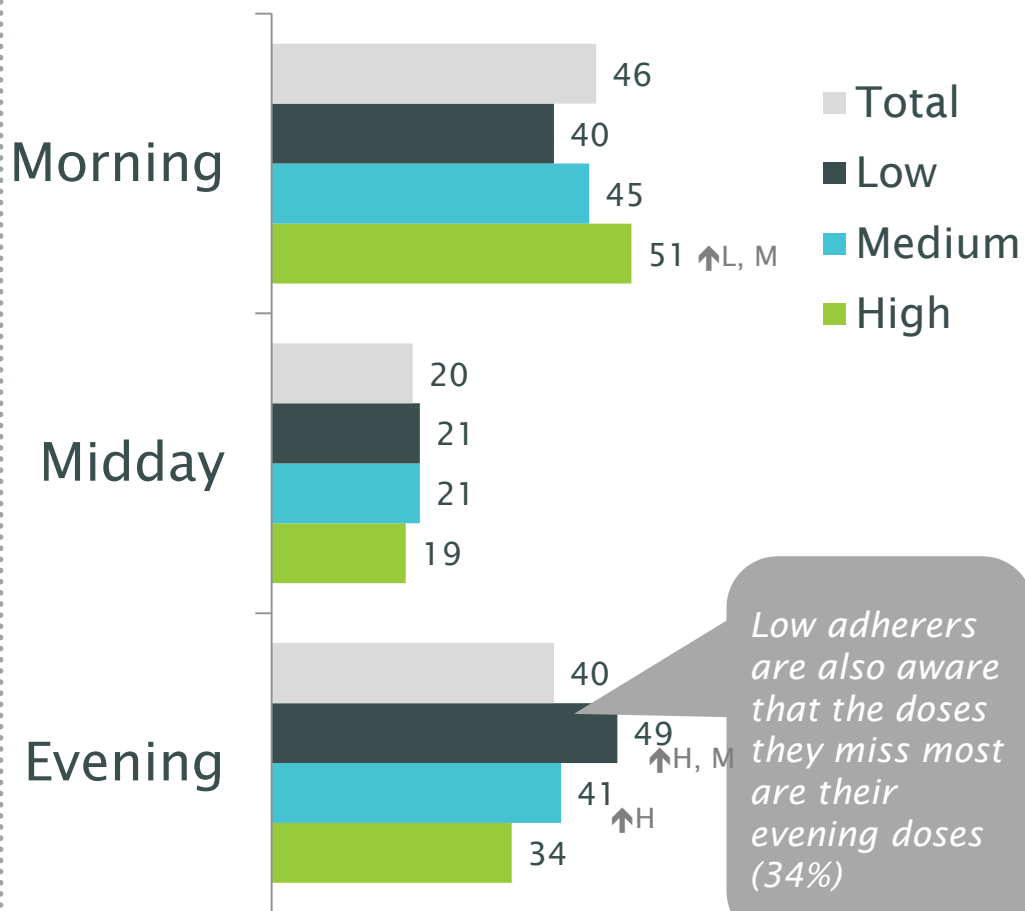
B3a / base-all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - Which medication do you take for your CML currently? B3a/B6 / base=all respondents (n=2546) - Which medication do you take for your CML currently? What CML treatments, if any, did you have before you began to take the one you are currently taking?

# Those with low adherence are more likely to take their medication 2 x day & do so in the evening

How many times take medication % / Av.



Time of day that take medication %



B4a / base=all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How many times a day do you take your CML medication? B4b / base=all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - When during the day do you usually take your CML medication?



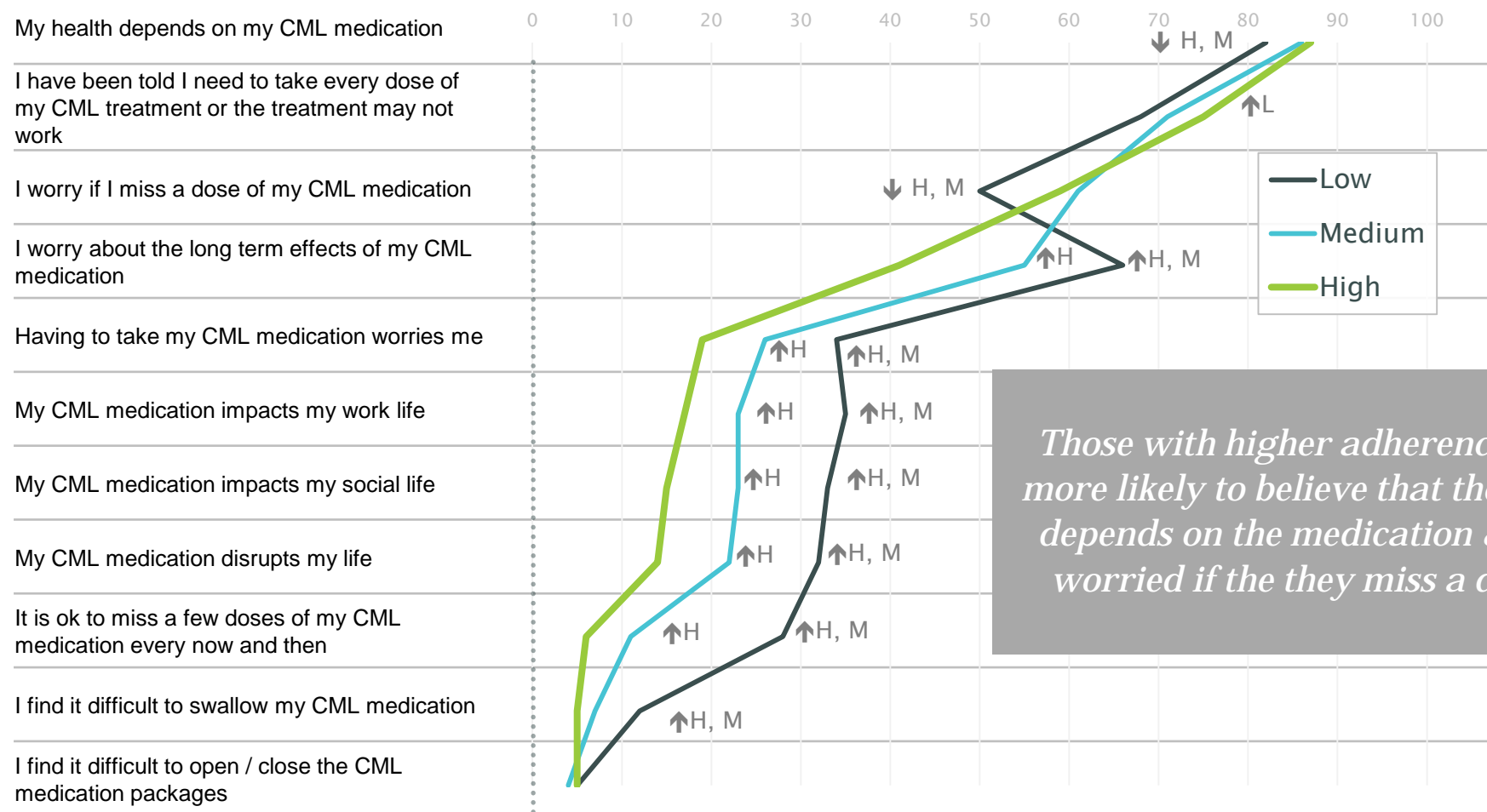
---

# Beliefs & Motivation



# The low adherence group perceive their QoL to be affected & worry about the long term effects of meds.

## Attitudes towards CML treatment by adherence groups (top 3 box%)

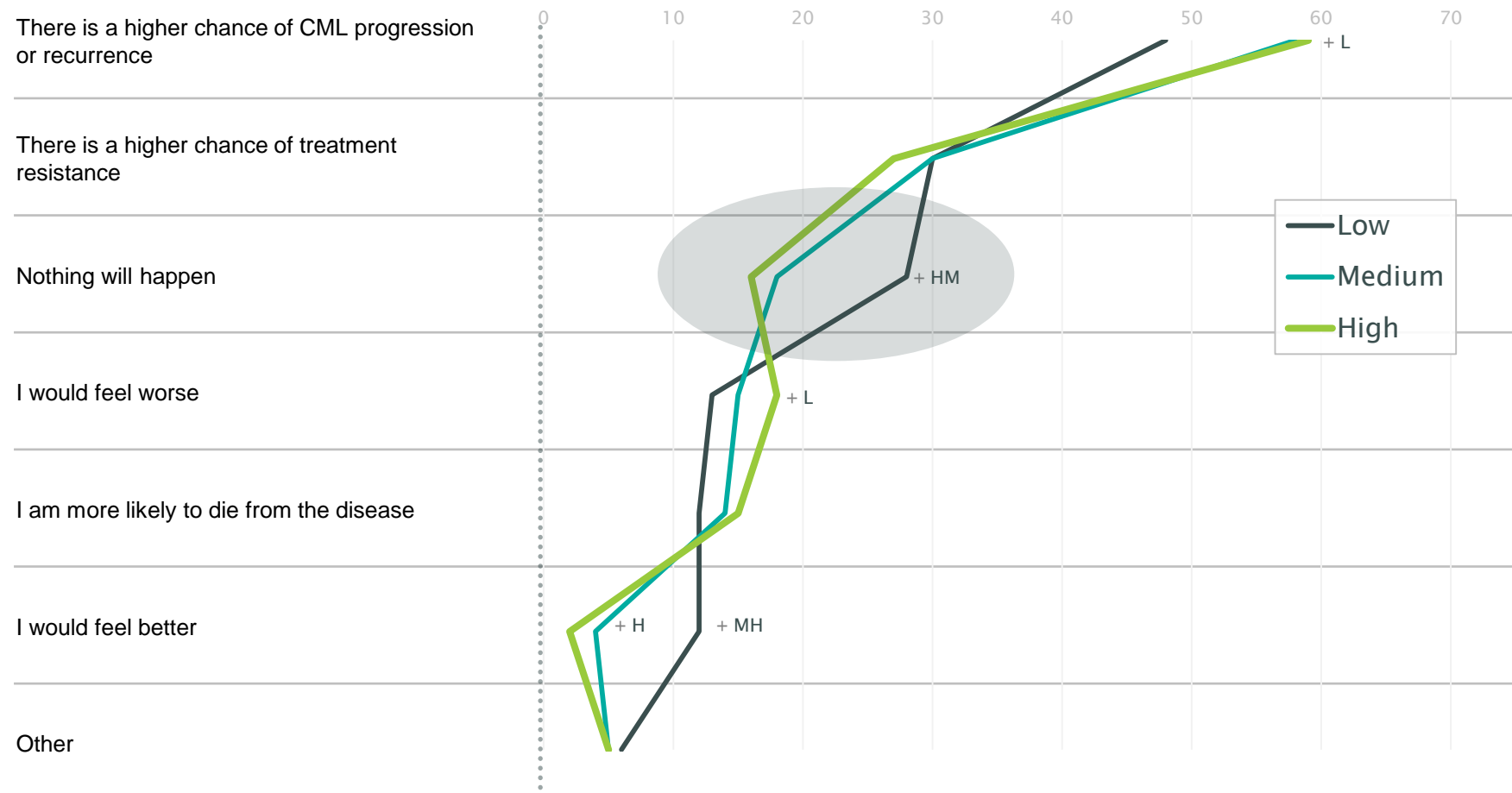


*Those with higher adherence are more likely to believe that their life depends on the medication & are worried if they miss a dose.*

C8 / base=all respondents (n=2546). Low (n=528), Medium (n=1185), High (n=833) When thinking about your CML medication, please indicate the extent to which you agree with each of the following statements? (Please indicate for each item below on a scale of 1-7 where 1=strongly disagree and 7=strongly agree)

# Those with lower adherence are less likely to understand the consequences of missing a dose

## What would happen if missing a dose of CML medication within a month



D6 / base=all respondents (n=2546). Low (n=528), Medium (n=1185), High (n=833) What do you think would happen if you miss one or more doses of your CML medication within the space of a month?



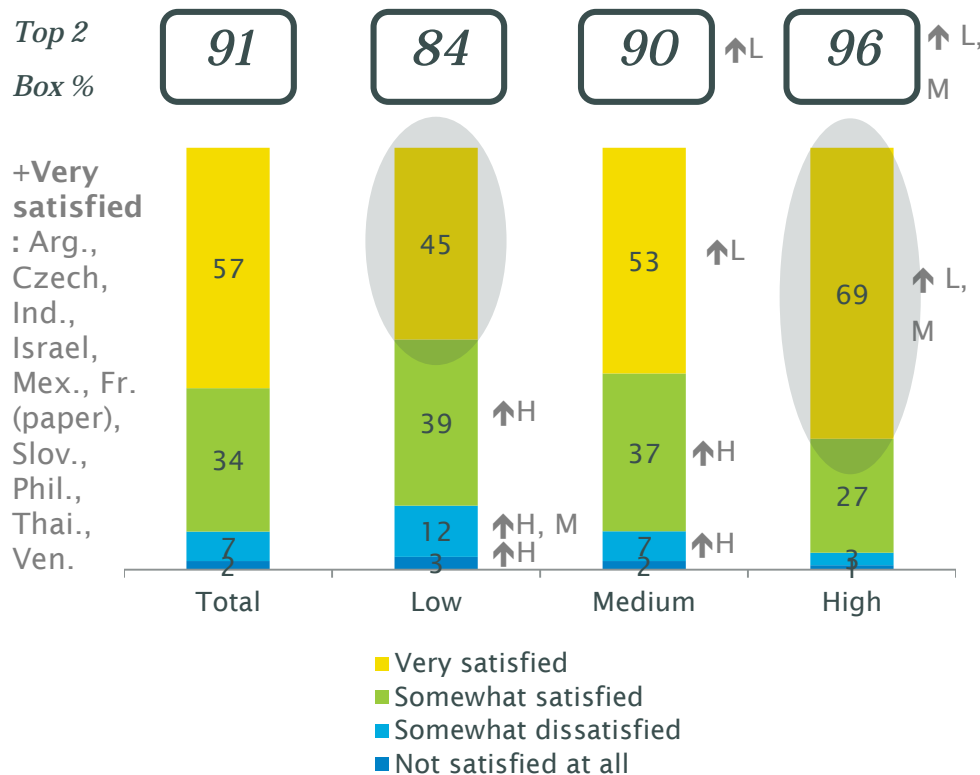
---

# Meaningful relationships

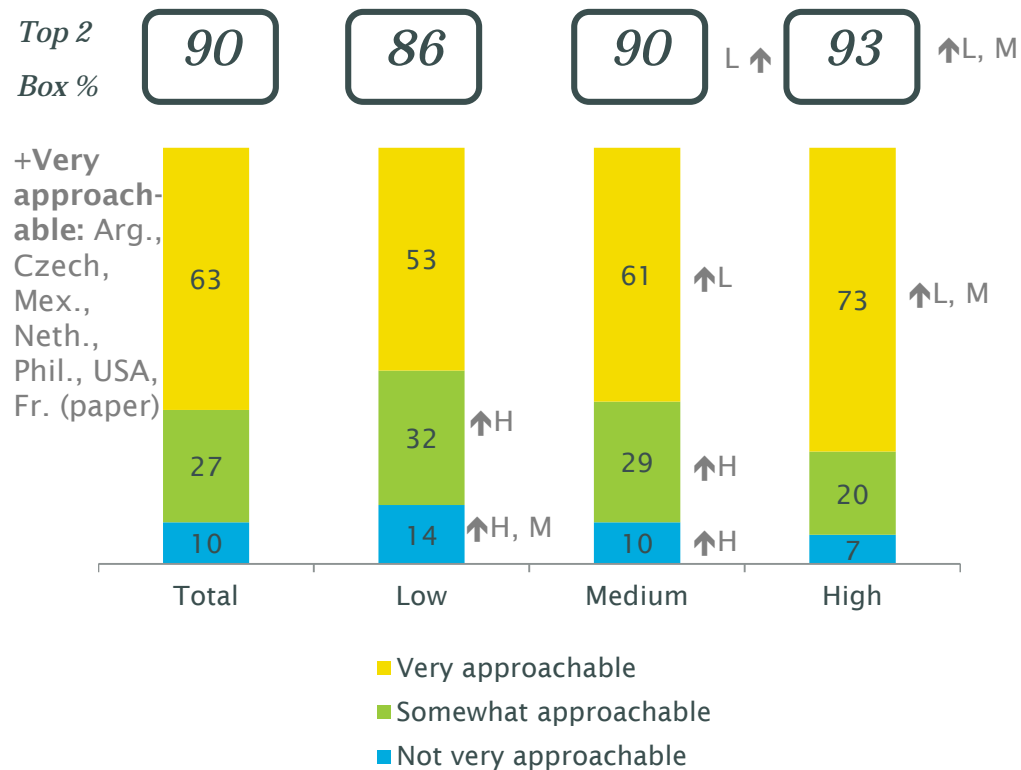


# Those with higher adherence are also more satisfied with info. & perceive their HCPs to be approachable

## Satisfaction with information received from CML doctor about CML and how it impacts your life



## Perceived approachability of CML doctors



D1b/ base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How satisfied are you with the information you receive from your CML doctor about CML and how it can impact your life?; D2 / base = all respondents (n=2546) Low (n=528), Medium (n=1185), High (n=833) - How approachable do you find your CML doctor is in terms of discussing the challenges you may be facing in taking your CML medication?





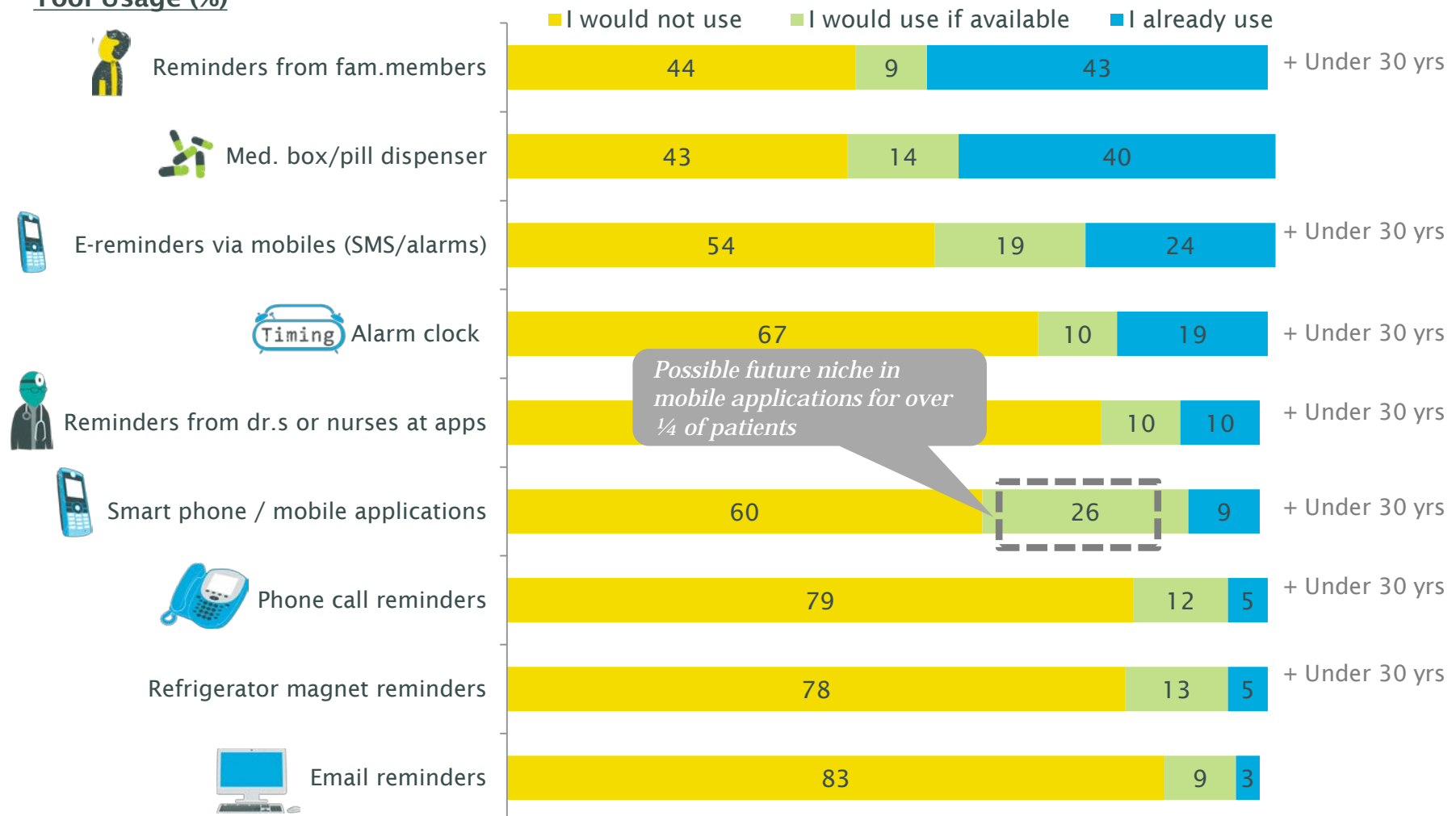
---

# Strategies for Adherence



# Reminders from family members & dispensers are the primary tools used, followed by electronic reminders

## Tool Usage (%)



E2 base = all respondents (n=2546) Below is a list of tools that could help you to remember to take your CML medication. For each item, please indicate whether you already use such a tool, or if you would use the tool if it were available



# Conclusions & Recommendations

# Recommendations (i)

---



- Could physicians be provided with materials to remind them of their central role in adherence?
- It is important that they are approachable & open to discussing the impact of medication on patients lives (side effects & quality of life) and any possible strategies patients can employ to overcome this.



- Particular attention should be paid to patients that are “more at risk” of non-adherence:
  - The younger patients
  - Those on nilotinib & on later lines
  - Those who have to pay & travel to get their medication

## Recommendations (ii)

---



- **Shifting attitudes** amongst those with low adherence will also help – some form of educational campaign could emphasise the importance of adherence.
- The **positive impact of routine** could also be highlighted (perhaps a link with the morning routine?) and could be conveyed through this campaign.
- We already have some powerful imagery that could be utilised in messages, coming from the patients themselves: *“I wouldn't forget to get dressed - same principle!”*



- Some evidence that there is **future potential for adherence tools** such as smart-phone apps & text messages
- However these should be less of a priority than the change of mind-set required amongst those with low adherence.



# 18<sup>TH</sup> CONGRESS OF EHA

STOCKHOLM

SWEDEN

JUNE 13 - 16

2013

Join us for the  
oral session in the EHA  
scientific programme  
on Sunday 16 June  
8:45-9:00

## Abstract Submission

**08. Chronic myeloid leukemia - Clinical**  
EHA18ABSSUB-4375

**NON-ADHERENCE IN CHRONIC MYELOID LEUKEMIA: RESULTS OF A GLOBAL SURVEY OF 2546 CML PATIENTS IN 79 COUNTRIES**

Giora Sharf<sup>1,2\*</sup>, Verena Hoffmann<sup>3</sup>, Felice Bombaci<sup>4</sup>, Mina Daban<sup>5</sup>, Fabio Efficace<sup>6</sup>, Joëlle Guillhot<sup>7</sup>, Jana Pelouchová<sup>8</sup>, Euzebiusz J. Dziwinski<sup>9</sup>, Jan de Jong<sup>10</sup>, Anthony Gavin<sup>11</sup>, Jan Geissler<sup>1,12</sup>

<sup>1</sup>Leukemia Patient Advocates Foundation, Bern, Switzerland, <sup>2</sup>Israeli CML Patients Organisation, Netanya, Israel, <sup>3</sup>

Institute of Medical Information Sciences, Biometry and Epidemiology (IBE), LMU, Munich, Germany, <sup>4</sup>Gruppo ALL

Pazienti Leucemia Mieloide Cronica, Rome, Italy, <sup>5</sup>LMC France, Paris, France, <sup>6</sup>Data Center and Health Outcomes

Research Unit, Italian Group for Adult Hematologic Diseases (GIMEMA), Rome, Italy, <sup>7</sup>Insem CIC 0802, University

Hospital of Poitiers, Poitiers, France, <sup>8</sup>Diagnoza CML, Prague, Czech Republic, <sup>9</sup>Polish Nationwide Association for CML

Patients Aid, Warsaw, Poland, <sup>10</sup>Stichting Contactgroep Leukemie, Utrecht, Netherlands, <sup>11</sup>Leukaemia CARE, Worcester,

United Kingdom, <sup>12</sup>LeukaNET e.V., Riemerling, Germany

Please indicate your presentation preference: Oral Presentation

Has the submitted material been published in a journal (printed or online)?: No

Has the submitted material been presented or submitted to another event?: No

Do you wish to apply for a Travel grant?: No

**Background:** Optimal adherence to oral chronic myeloid leukemia (CML) therapy is of key importance to maximise treatment effectiveness. Non-adherence as well as its biological effect on CML has been observed in clinical research, but data on potential driving factors of non-adherence are lacking in the scientific literature.

**Aims:** The aim of this study is to investigate motivations and behavioural patterns of adherence in CML and subsequently support hematologists and patients to improve adherence and develop suitable adherence tools.

**Methods:** A European workgroup of the CML Advocates Network, a network of leukemia patient groups in 55 countries, has conducted a large international study enrolling patients from 09/2012 to 01/2013 in 12 languages. The study was also supported by CML investigator groups in Germany, Italy and France. An *ad hoc* questionnaire was developed for the purpose of this study and this included questions on potential factors associated with non-adherence and other aspects related to patients' perception of disease and treatment burden. Also, medication taking behavior was assessed with the 8-item Morisky Medication Adherence scale (MMAS-8). This scale allows classification of patients into their level of adherence to treatment (i.e. low, medium and high adherence). Patients completed this questionnaire online. An additional sample of patients were given this questionnaire, along with a pre-stamped envelope, by their own treating physicians in hospital with the request to completing it at home. These questionnaire were then returned to an independent Data Center for analyses. Differences in adherence groups were determined by  $\chi^2$  tests, differences of mean adherence were determined with Mann Whitney U tests and Kruskal Wallis tests.