




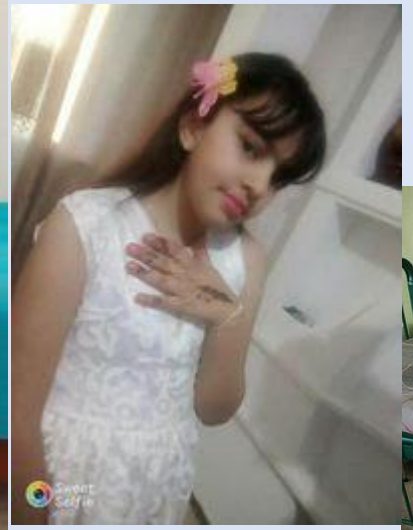



More Mornings for CF Warriors in Developing Countries

Improving Quality and Length of Life by Enhancing Access to Basic, Evidenced Based CF Care

Presenters:

Mark A. Tremblay, M.A., M.P.A.

President of CF Vests for Life and CFV4L – since June 2020.

Helped improve access to evidenced based, basic CF care for more than 300 families around the world

- 6 years - Team Leader in NYS Governor's Division of Budget

- 25 years – Department of Health Medicaid Data Unit Manager

Jacob A. Venditti

Founder of Live Fearlessly Foundation

Helped people with CF follow their passions for activity by awarding 140 activity grants to patients all over the world

Collaborated with CFV4L to provide 8 families with evidenced based medication such as digestive enzymes and CF multivitamins in developing countries.

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- Donor environment
  - 90% of patients in the US and other first world countries (USA, UK, Ireland, Denmark, Germany, Slovenia, and Lithuania) have access to Highly Effective Modulator Therapy (HEMT) and have experienced a significant reprieve in symptom acuity and disease progression which is supported by the recent median increase in US CF life expectancy to 50 years of age and precipitous drop in CF lung transplants
  - With the introduction of HEMT, many have experienced significant improvements in their physical health and quality of life so patients, caregivers, and clinicians have begun to shift their focus from mere survival to higher order concerns like emotional, psychosocial and mental wellness
  - Further, there is more hope than ever that burdensome treatment regimens will be replaced with a few pills a day for patients on HEMT. The literature has begun to reflect this optimism as well, as more studies are being conducted on the effects of streamlining treatment protocols including: eliminating nebulized medications, therapy vest treatment, and IV antibiotics. In fact, many such research projects are already underway (e.g., CFF is reaching out to arrange focus groups)
  - This is an opportunity to empower many patients and families who have historically been recipients of services so that their medical privilege and their pursuit of higher order concerns may spur them to help their fellow warriors in the broader global community who lack access to basic care.

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- **Recipient environment**
  - **Nearly all southern and third world countries do not have access or public funding for HEMT (e.g., Trikafta, Symdeko, or Orkambi)**
  - **Many countries (e.g., India) devastated by the COVID-19 pandemic have experienced serious depletions in resources which has made airway clearance devices (therapy vests, Aerobikas, Flutterers) and Oxygen devices (POCs) inaccessible to most CF patients**
  - **Additionally, areas of the world where enzymes were widely available (Tunisia, Mexico, and Iran) are now experiencing severe shortages due to decreased manufacturing capacity and plant closures during the COVID-19 pandemic**
  - **CF treatment to most developing countries is on par with treatment in the US in the 60s and 70s except that in many cases digestive enzymes are not available**
  - **Consequently, life expectancies in many areas of the world are less than 10 years of age (e.g., Gaza Strip, Tunsia, India, Ecuador, and Mexico)**
  - **The mix of Delta F508 (monozygotic or dizygotic) and nonsense genes varies from the US so HEMT is not an option**

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CF Treatment Comparative Efficacy Analysis and Humanitarian Aid Viability for Developing Countries

Treatment Efficacy and Viability

Therapy/Intervention	Cost	Transportation	Efficacy	Source and Access	Strengths/Weaknesses
Saline Solution for Nebulized Inhalation (3-7%)	Nominal up front, fixed cost for beaker and supplies	NA	Highly effective	Can be produced at home	Generally is not well tolerated by patients with low lung volume or high acuity exacerbations (e.g., hymoptisis, pneumothorax, and vomiting)
Pulmozyme	$24,000 USD annual cost	Temperature controlled,refrid-gerated transport and storage	Highly effective	Manufactured in plant	Expensive, hard to transport, but easily tolerated
Albuterol	$1,200 USD annual cost	Light, easily transported	Nominally effective	Manufactured in plant	Easy to transport, easily tolerated, but minimally effective

Treatment Efficacy and Viability

Therapy/Intervention	Cost	Transportation	Efficacy	Source and Access	Strengths/Weaknesses
Therapy Vests	$2,000 to $14,000 USD one-time cost	Hard to transport due to weight and VAT. Most shipments require couriers for transport	Highly effective if used correctly in combination with training and basic airway clearance techniques	High tech, manfactured, can be unrelaible, voltage variability, electric current instability can easily cause equipment damage and repairs are costly or unavailable. However, supply is increasing in first world countries as HEMT has reduced utulization and demand	Best tolerated by patients with higher lung functions (+20% FEV-1), expensive, reliability issues in developing countries and sensitive to black market sale
Aerobika or Flutterer device	$75-125 USD one-time cost	Light, durable and easy to ship directly to provider	Highly effective combined with training, basic airway clearance and pulmonary rehab techniques	Manufactured but readily available	Requires training and education component to be as effective as other airway clearance techniques. Educational content and materials easy to access online (e.g., Physio Inc)

Treatment Efficacy and Viability

Therapy/Intervention	Cost	Transportation	Efficacy	Source and Access	Strengths/Weaknesses
Healthy nutrition with/without macronutrient supplementation (i.e., protein shakes)	$600-1,200 USD annual ($50-$100 per month)	NA	Effective but requires education and training	Nutritious food available within patient community	Requires training, education and would best be implemented with online telemedicine or train the trainer remote or in person model
Fat soluable vitamin supplementation	As little as $240 annual cost ($20 per month)	Heavy, costly to ship, challenging to find couriers	Effective if taken long-term	Generally available locally or online at nominal cost	Bottle of vitamins is equivalent in weight, size and cost to 3 months of enzymes. Makes it hard to recruit couriers
Pancreatic Enzyme Replacement Therapy (PERT)	As little as $1,440 annual cost ($120 per month for most patients)	Easy to ship directly or through courier	Highly effective particularly for 90% of patients w/ EPI and especially for the 20-30% of pts. w/ siginficantly low BMI	Direct donations difficult to obtain. Significant monetary donations would be needed to procure. Global access decreased since COVID-19 due to global production cuts	Great ROI for areas where patient access to PERT is too costly or inaccessible in terms of marginal cost vs. relative efficacy

Treatment Efficacy and Viability

Therapy/Intervention	Cost	Transportation	Efficacy	Source and Access	Strengths/Weaknesses
Airway Clearance Education and Training	Online access but does require access to internet and/or telemedicine platform at recipient site	NA	Highly effective, could benefit the majority of patients regardless of acuity or chronicity	Content would have to be produced and diseminated primarily in first world countries where mature well-resourced CF nutrition programs exist. However, significant existing content could be leveraged to mitigate production costs	May require intial provider investment. Could be more effective if coupled with telemedicine and even more effective if motivational interviewing principles were employed
Antibiotics, IV	Difficult to procure, can be extremely costly, $80-$40,000 USD per course of antibiotics	Requires refridgerated, temperature control transport and storage	Highly effective, particularly for acute exacerbations	Would be unrealistic for most international NGOs because you would likely need a pharmicist or doctor to adjust drug dosages for each patient. More widely avaiable than would be assumed	Extremely difficult to ship, dose and type need to be adjusted for each patient, IV antibiotics in facilties with high iatrogenic illness prevalance and low staffing can carry additional risks of serious side effects (e.g., blood infections) and antibiotic resistance
Antibiotics, Oral	Patients have to dispose of bottles of unused pills once opened, so there are no excess enzymes to donate	Requires temperature controlled transport and storage	Highly effective depending on sensitivities	Could be purchased and prescribed here for patients overseas or by provider directly. Also, requires on-site pathology lab and additional resources for side effect management. Widely avaiable globally	Cost is low, would be hard to implement due to physician/pharmicist requirements in the US

Treatment Efficacy and Viability

Therapy/Intervention	Cost	Transportation	Efficacy	Source and Access	Strengths/Weaknesses
Tobi Podhalers	Extremely expensive $12,000 for single one month supply. Small quantities of donor inventory available in the US	Requires temperature control transport and storage	Highly effective for patients w/ certain IDs including PA prevalant in 80% of patients in overseas clinics	Only two options for sourcing: would have to be purchased and prescribed in the US for patients overseas or would have to be donated by patients who have excess supply. Also, requires additional resources for sputum culture analysis	Donated Tobi Podhalers could be provided to a small number of patients primarily with PA in developing countries
Long term HEMT (e.g., Trikafta)	$270,000-$330,000 USD annual cost, miniscule donor supply	Easy to transport and ship directly	By far the most effective treatment option currently available	Supply is extremely limited and the only viable option for donation is patients in the US with excess supply	Available government and private resources make this option unrealistic for most developing countries where providing these medicaitons to eligible recipients would consume a sizable chunk of the national healthcare budget
Short term HEMT acute or resistant infections (e.g., Orkambi, Symdeko)	$22,000 USD for month supply, significant donor supply in circulation in the US	Easy to transport and ship directly	Highly effective, particularly when combined w/antibiotics	Significant supply of older generation modulators available subsequent to the widespread of Trikafta	Is highly effective to treat acute exacerbations particulary if combined with antibiotic therapy

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Inequities in Access: Modulators, PERT, Airway Clearance, HEMT, and Effective Antibiotic Treatment by Region and Country

Access Inequities by Region and Targeted Country

Region	Est # of diag. Patients (Jonathan Guo et al.)	Countries	Est # of pts in country based on live births Prevalance (Luiz Vicente Ribeiro F. Silva Filho et al.)	Modulator Access	Airway Clearance Device Access (Therapy Vests, Aerobikas, Flutters)	Number of Pts who lack access to ariway clearance devices	Digestive Enzymes	Number of Pts who lack access to CF enzymes	Infectious Disease Treatment (IV, inhales and oral antibiotics)
North America	37,000	US		Y	Y	0	Y		Y
		Canada		Y	Y	0	Y		Y
		Mexico, Caribbean	5,294	N	N	2,647	Severe shortages	2,647	Limted range and access, no inhaled Tobi or Caystin
		Central America	21,000	N	N	10,500		10,500	
South America	10,000	Brazil	15,429	N	N	7,714	Limited supply, patients pay	7,714	Limted range and access, no inhaled Tobi or Cayston
		Argentina	6,571	N	N	3,286	N	3,286	
		Cuba	3,000	N	N	1,500	N	1,500	Extremely limited access
		Ecuador	4250	N	N	4,250	Gov ins does not pay for	3,400	
		Other		N	N	0			
Europe	47,650	EU		Y	Y for adults	9,530	Y	0	Y
		Ireland, Denmark, Germany, and Slovenia		Y	Y for adults		Y	0	Y
		Lithuania	667	Y	Y	0	Y	0	Y
		Ukraine	12,333	N	N	6,167	Very limited supply, cost bourn by partients, black market access	7,400	Limted range and access, private payers have access, poor have no access
		Russia *	48,000	N	N				
Subtotal Diagnosed	94,650					45,594		36,447	

Access Inequities by Region and Targeted Country

Region	Est # of diag. Patients (Jonathan Guo et al.)	Countries	Est # of pts in country based on live births Prevalance (Luiz Vicente Ribeiro F. Silva Filho et al.)	Modulator Access	Airway Clearance Devices (Therapy Vests, Aerobikas, Flutters)	Number of Pts who lack access to ariway clearance devices	Digestive Enzymes	Number of Pts who lack access to CF enzymes	Infectious Disease Treatment (IV, inhales and oral antibiotics)
Australia & New Zealand	3,650			N	Y	0	Y	0	Y
Asia	5,350			N	N	4,280	Very limited access, cost bourn by patients	2,675	Limted range and access, private payers have access, poor have no access
		India	14,258	N	N	13,545	Cost of vest 6 months salary	13,545	Biggest challenge in CF tx. Pts ration - take less than rec
Africa	1,670			N	N	1,503	Almost no access, an estimated 20% have access and	1,587	Limted range and access, private payers have access, poor have no access
		Tunia and Algeria	3,000	N	N	2,700	N	1,500	Limted range and access, private payers have access, poor have no access
		South Africa (assumed in 1670 Africa pt total)	523	N	N	518	Y		Limted range and access, private payers have access, poor have no access
Subtotal Diagnosed	10,670					22,546		19,307	
All Country Total	105,320					68,140		55,754	

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What can the international NGO and private non-profit community do to make a difference?

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- **Tried and true public policy and one off approaches to improve CF patients' lives in developing countries**
  - **Advocate so that countries add HEMT to their government formularies and sufficient funds to procure and supply drug to the CF population**
  - **Advocate for drug manufacturers to sell products under externally imposed drug caps or undertake targeted benevolence initiatives**
  - **Advocate for countries to increase per capita government health care spending to improve access to non-modulator treatments**
  - **Provide direct to patient assistance with critical, much needed Durable Medical Equipment (DME) and medication in areas where access is limited or non-existent**
- **Population health or public health approach to improving CF patient's lives in developing countries**
  - **Work to support doctors, clinics, and hospitals in their efforts to meet their patients' needs through education, staff training, providing DMEs (for lease to patients), and critical, evidenced basic CF medication, and nutritional support**

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- **Most cost effective, treatment interventions, based on cost, ease of implementation and on site clinical viability**
  - **Produce and disseminate training materials for saline inhalation solution tailored to clinicians and patients in developing countries so that more CF patients can produce this simple yet powerful treatment safely and administer it independently**
  - **Increase access to Aerobikas, Flutters and other simple low cost airway clearance devices and provide the necessary training materials and programs to utilize them effectively**
  - **Produce and disseminate training materials to teach clinicians and patients basic pulmonary rehab concepts including how to huff cough, “feel” areas of acute pulmonary congestion, and target congested areas, as well as exercise for pulmonary optimization etc.**

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- **Most cost effective, treatment interventions, based on cost, ease of implementation and onsite clinical viability (cont.)**
  - **Provide more airway clearance devices to patients utilizing stepwise approach (e.g., if the Aerobika with proper training is not working try vest). Providers lease high tech DMEs (therapy vests, Portable Oxygen Concentrators, and nebulizers) to patients. If patients can no longer use DME it is returned to provider for disinfecting and redeployment. Increase access to PERT for patients that can not afford or do not have access**
  - **Increase access to CF multivitamins where/when it is cost prohibitive**
  - **Increase access to PERT through monetary contributions ($120 USD per month; $1,440 per year)**
  - **Increase awareness and provide training to improve overall health through nutrition and exercise for patients**

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Airway Clearance Treatment Bundle

- Produce and disseminate training materials for inhaled saline solution tailored to clinicians and patients in developing countries so that more CF patients can produce this powerful treatment safely and administer it effectively independently
- Increase access to Aerobikas, Flutters and other simple low cost airway clearance devices and the accompanying training materials
- Utilize stepwise approach to issuing vests and have doctors enter into to lease arrangements with patients and families to mitigate black market resale risk
- Produce and disseminate training materials to teach clinicians and patients basic pulmonary rehab concepts including how to huff cough, feel and target congested areas in the lungs, exercise for optimal pulmonary gain etc.

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PERT and Nutrition Treatment Bundle

- Increase access to PERT for patients that can not afford or do not have access to digestive enzymes
- Increase access to CF daily multivitamins
- Increase awareness and provide training and coaching to improve patient health through nutrition and exercise

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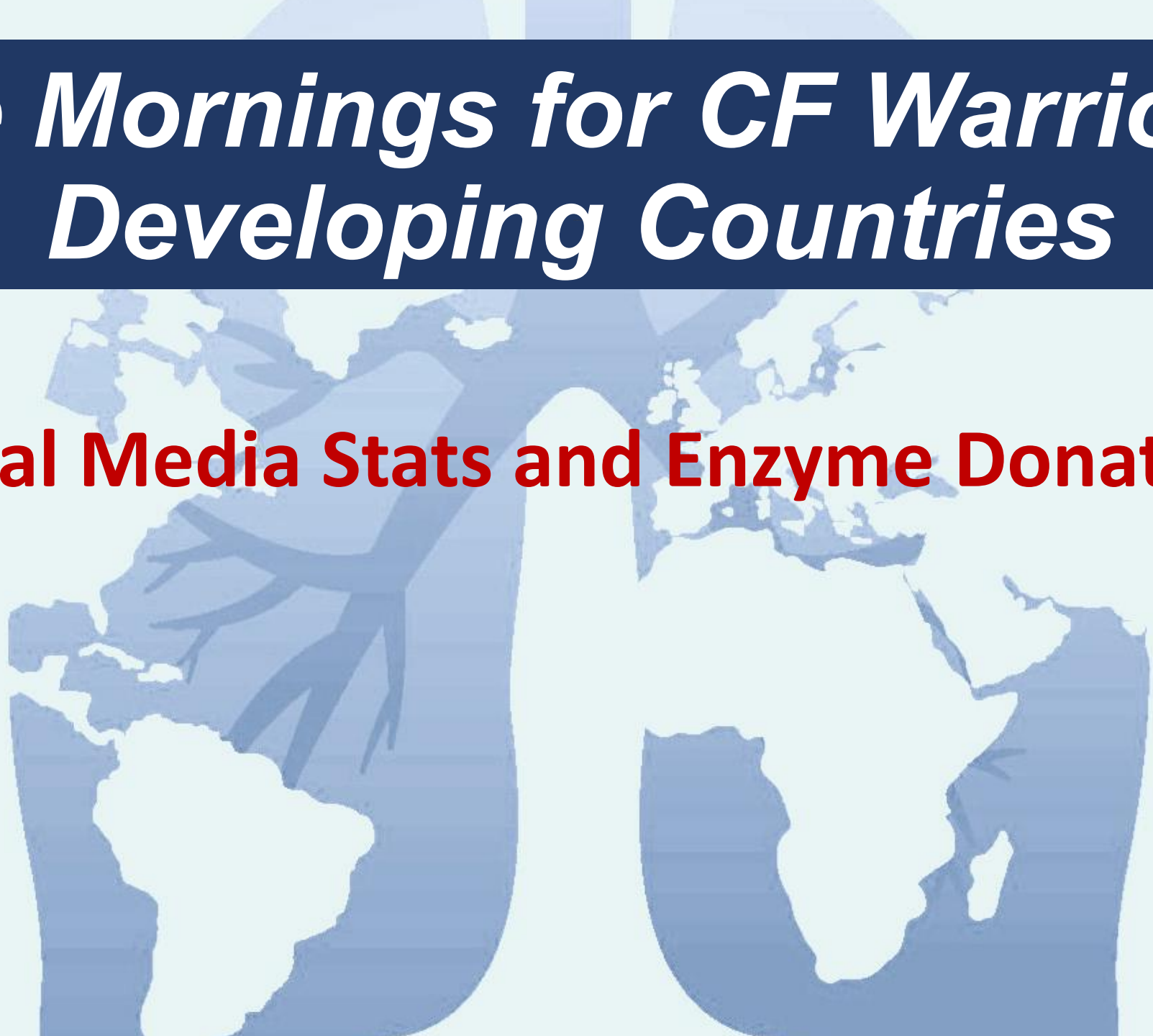
Social Media Stats and Enzyme Donations



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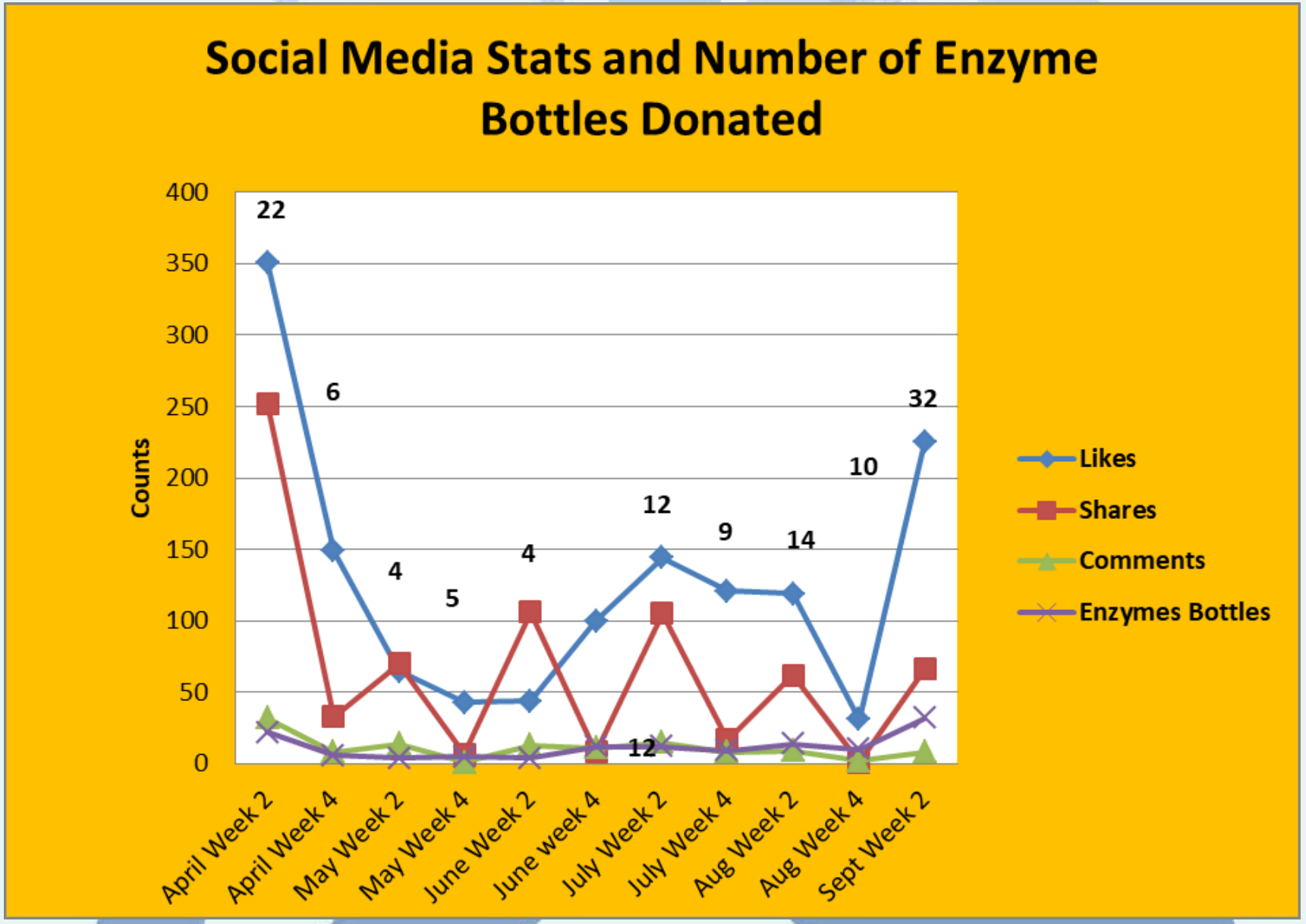

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APPENDIX AND NOTES:

- Guo, Jonathan, Garrett, Anna, Hill, Andrew (2022), Worldwide Rates of Diagnosis and Effective Treatment for Cystic Fibrosis, Journal of Cystic Fibrosis www.elsevier.com/locate/jcf
- Filho, Luiz VicenteRibeiro F. Silva, Castanos, Claudio, Ruiz, Hector Herman, Cystic Fibrosis in Latin America-Improving the Awareness (2016), Journal of cystic Fibrosis, 15, 791-793
- Wikipedia, List of Countries by Total Health Expenditures Per Capita
- OpenAI (2023) ChatGPT (Sept 23 Version) https://chat.openai.com/chat
- Zampolli, M, Verstraete, J, Frauendorf, M, et.al. (2021) South African Cystic Fibrosis Patient Registry. https://sacfa.org/ZA/

- We lost contact with our Russian pulmonary clinics on April 3, 2023, but in light of the prevalence of CF relative to live births in the country there may be as many as 40,000 CF patients that reside there as much as half of whom do not have access to basic or high tech airway clearance devices and PERT

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Questions